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THERAPEUTIC RADIOLOGY*

PRESIDENT'S ADDRESS

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IT HAS been a pleasure and a privilege to serve as President of the American Radium Society during the past year and to carry out the duties which normally go with this office. It is also a pleasure to deliver this Presidential Address as it affords an opportunity to philosophize on a subject which is important to the future of therapeutic radiology.

It is motivated by a conviction that the results from the radiation treatment of cancer are not always as good as they should be, and that they would be improved if patients with cancer always received the best that irradiation has to offer. Patients with cancer expect the best treatment available, and when the modality chosen is irradiation, it is the radiologist's responsibility to see that they obtain the best in his field. This field is a large one because radiation therapy in the hands of the well trained and experienced physician stands equal with any other procedure as a primary treatment for cancer, and it plays a major role in the treatment of incurable, recurrent, and terminal phases of malignant diseases as well. All told, many cancers are treated by radiation, and it is doubtful if anyone plays a greater part than the radiologist in the over-all management of the cancer patient, unless it be the general practitioner.

The radiologist, therefore, has serious responsibilities in planning for radiation therapy because the difference between the administration of good and poorly planned radiation therapy may be a matter of life or death, of cure or failure, or may indeed spell the difference between palliation and aggravation of symptoms.

Before the radiologist is prepared to meet these responsibilities in a forthright manner, he must first be taught by the teachers of therapeutic radiology what his responsibilities are. These teachers must, therefore, indoctrinate the postgraduate trainee in the importance of giving cancer patients in the community where he practices the best advice about radiation therapy, regardless of whether facilities for the preferred treatment of a specific problem are available locally or elsewhere.

It is necessary that residents in radiology be thus instructed because a large proportion of radiation therapy is given by radi-

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ologists who practice therapy as a part time interest with the facilities which they have available, even though they may not always be adequate.

There are many hospitals in small communities where qualified personnel and facilities for irradiation are comparatively limited. In some, the personnel is limited to a radiologist and a technician, in others, even they are only part time workers. Consequently, the therapy patient may of necessity be seen briefly by the radiologist between roentgenographic readings or fluoroscopies. With a practice of this sort, the radiologist may have only a limited interest in radiation therapy, either because he does not have enough patients to occupy him completely, or because he is more interested in other aspects of radiology, or because other phases demand so much of his time that he has little left for therapy. Regardless of the reason, part time attention to radiation therapy, no matter how well done, can be frustrating and it may be a major reason why statistics from irradiation vary as they so often do from one place to another.

These are some of the reasons why there is a trend for full time radiotherapists in those places which can support them and why specialization in therapeutic radiology is not only desirable but necessary. This does not necessarily mean that full time radiation therapy is always good, and that part time radiation therapy may not be so good. We all know that many important contributions to scientific medicine have come from small laboratories and from part time workers. But it is certain that unless the best therapeutic radiology is practiced, a very valuable therapeutic agent for the treatment of cancer may become discredited in those areas where it is done poorly.

A collaborating program between hospitals with limited facilities and fully equipped and staffed radiation centers would improve substandard results. Such a program would make available high level consultation together with complete facilities for every irradiation problem. Programs of this nature, wherever integrated, would aid in improving end results from radiation therapy and statistically these would then compare favorably with the best ones reported.

End results, however, are not likely to improve unless radiotherapists know their own results and how they compare with the published data of others. It is not enough for the radiologist to proclaim the superiority of irradiation in the treatment of cancer over some other recognized treatment by pointing to outstanding statistics of others. He should be able to show that his own results are as good, or better, than those obtained from other methods of treatment in the community where he practices.

Some of the best results are reported in statistics from large centers, abroad and in this country, where radiation therapy is a full time specialty. These centers usually have adequate resources with which to acquire the facilities needed for the best irradiation. They are most likely to be able to afford outstanding therapists, physicists and others who know how to make the best use of the facilities. They are also most likely to have a large number of patients with all kinds of cancer in all stages of the disease to provide ample material for teaching, for research and for compiling a sizable volume of records. In centers like these, patients with cancer are most likely to get careful evaluation and individualized treatment. Accordingly, the end results should be the best and they usually are.

It is not the intent of this address to decry radiation therapy in small hospitals or in private offices. These places are most important and essential to the economy of radiation therapy. Neither is it intended to infer that all patients with cancer who require radiation therapy should of necessity be referred to radiation centers, nor that a radiologist is less competent because he is not in a large center, nor that therapy facilities in one place do not have the same potential as in any other place. It is intended, rather, to imply that limitation of facilities

should be recognized and not exceeded, and that those who use the facilities become dedicated to the principle that every patient with curable cancer should receive the best that irradiation has to offer even if it is necessary to send the patient somewhere else to get it.

There should be no reluctance on the part of institutions to refer patients elsewhere because of pride that their institutions are self sufficient, nor should the radiologist submit to pressure from patients or anyone else to do other than that which he thinks best. It should be recognized that it is neither practical nor economical for every community hospital to be fully equipped with all the available therapeutic facilities, and have the trained personnel that would be needed for selective treatment of every kind of cancer. The public could not afford it and the experienced personnel are just not available. Nevertheless, other adequately equipped and staffed centers, besides those now available, are needed where patients requiring selective therapy can be referred.

Integrated consulting programs between radiation centers and community hospitals would make available good advice and good therapy for all who need them. Such programs would educate the physician and the public to the fact that radiation therapy embraces more than the technical procedure of placing a patient in a beam of radiation for a predetermined length of time. They would make clear that a knowledge of pathology, radiation physics, radiobiology, chemotherapy, the history of cancer, and many other things relating to malignant disease are necessary and vital for good radiation therapy. They would also make clear the need for full time radiotherapists in those places which can support them.

The purpose of this address is not to criticize but to emphasize that radiation therapy is still one of the most important methods for the treatment of cancer and that radiologists are charged with the obligation of using it well.

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A PRECISION COBALT 60 UNIT FOR FIXED FIELD AND ROTATION THERAPY*

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SINCE the first cobalt 60 beam therapy unit was installed in the University Hospital, Saskatoon, Saskatchewan, in August, 1951,[4] many types of cobalt 60 units have been constructed and placed in operation in various parts of the world. Some are good designs; some are poor. Some are designed for precision radiation therapy; others merely to sell. Some have very large penumbra; others have small penumbra and produce radiation distributions that cannot be distinguished, from a penumbra point of view, from those produced by a high energy roentgen-ray machine (1–4 mev.). In 1957 Kligerman *et al.*[7] at a symposium demonstrated that a cobalt 60 unit with a large penumbra produced radiation distributions in the head and neck region which were hardly distinguishable from those obtained from a 250 kv. roentgen-ray machine. Other participants[6] in the same symposium emphasized the importance of reducing the penumbra from a cobalt 60 unit to as small a value as possible. Penumbra can be minimized either by reducing the size of the source or by placing the diaphragm near to the skin surface or by a combination of both of these. To be practical, an isotope machine must produce field sizes of at least 20×20 cm., and when a diaphragm system capable of giving this field size is placed near the skin surface it can become very large and unwieldy unless special care is taken in its construction.

A multivane collimator of small external dimensions for collimating a cobalt 60 beam has been described.[3] A number of manufacturers have brought out small collimators which are based somewhat on the same principle. In all of these, the space between the skin surface and the source is used by the collimating device. It is almost impossible to adapt such a collimator to a cobalt 60 unit in which the space between the source and the skin is occupied by some other device such as the shutter mechanism.

In a recent article, Dr. Meredith[8] makes the following statement: "Thus although the radiocobalt telecurie unit has a place in a small radiotherapeutic center or when technical assistance is difficult to obtain, there seems to be no doubt that the linear accelerator operating in the region of 4 to 8 million volts is the best available machine for supervoltage roentgen therapy." Dr. Meredith bases his statement on a number of points, including large penumbra, low output, etc. In contrast to this point of view, the Ontario Cancer Institute in Toronto is equipped with three large cobalt units, one 1,300 curie cesium unit, one 250 curie cesium unit for head and neck work, and a 25 mev. medical betatron, as well as a few standard roentgen-ray machines. It is obvious that we lean very heavily on the use of isotope machines in this Institute.

Isotope machines have certain properties which make them unique in radiation therapy. Once the exposure rate has been measured accurately, it can be predicted with great precision from that time on. There are no problems of change in output with time, movement of a filter, etc. With cobalt 60 it is possible to reproduce year in and year out identical treatment conditions. This is essential if we are ever to unravel some of the clinical problems of radiation therapy. The advantages of cobalt 60 in this respect over linear accelerators and other supervoltage roentgen-ray machines should not be lightly thrown away through improper or careless design with respect to penumbra.

* Presented at the Fortieth Annual Meeting of the American Radium Society, Hollywood, Florida, March 27–29, 1958.
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DESCRIPTION OF UNIT

The general assembly of our cobalt 60 unit is shown in Figure 1. The head and counterweight are mounted on opposite ends of a hollow steel column, which rotates about a horizontal axis. The counterweight acts as a radiation shield, and a protective housing for the focussing ion chamber. The source is arranged to move horizontally as indicated in the diagram from the "off" to the "on" position. The end of the column next to the counterweight contains a 100 kv. roentgen-ray transformer which is connected to the roentgenographic tube mounted in the head. In general appearance the unit is somewhat similar to the theratron produced by Atomic Energy of Canada;[2] however, its physical dimensions are considerably larger. For fixed field therapy the device is arranged to treat at 80 cm., a distance which has proved to be the best compromise between high depth dose and a reasonable exposure rate for a cobalt 60 unit. For rotation therapy, the axis is placed at 93 cm. With these distances, even with minimum dimensions for the head, the axis would have to be about 125 cm. above the floor. To overcome this impractical distance from floor to axis, the unit is arranged so that when rotation occurs, the head passes below the floor level, as shown in the second view of Figure 1. The floor is equipped with two trap doors which move down when the system is set in rotation. The counterweight clears the true floor in all positions. When the patient is being "set up," the floor is completely level and unobstructed. When the rotation switch is turned on, the floor automatically goes down before the rotation starts. With this arrangement the axis of the machine is 100 cm. above the floor level, a convenient level for the "porting" of patients. The various optical light localizers are also shown in Figure 1. There is one which indicates the field size, one which directs a light beam to mark the "exit point" and two which project light beams at an angle to intersect at the center of the field at the treatment distance of 80 cm. The roentgenographic tube mounted in the head cannot be seen from the outside as it is completely embedded in the head. The roentgen-ray transformer mounted in the counterweight is excited through slip rings and a commutator. The device is arranged so that it can be rotated continuously in any one direction or set in oscillation. The whole device is mounted on I beams which are below the surface of the floor.

More details concerning the construction of the head are shown in Figure 2. A heavy

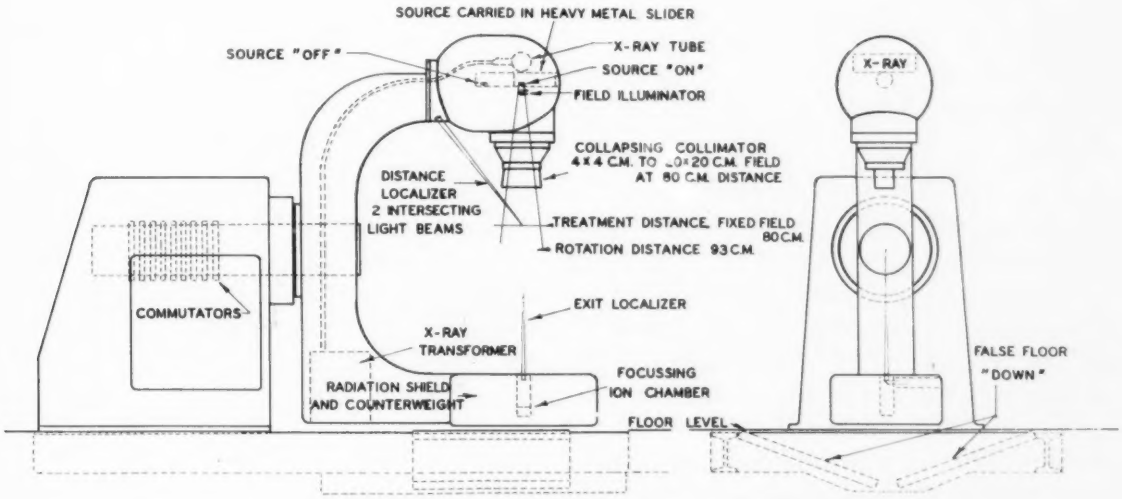


Fig. 1. A schematic diagram of the cobalt 60 unit showing the roentgenographic tube, the collapsing floor and the salient features of the device.

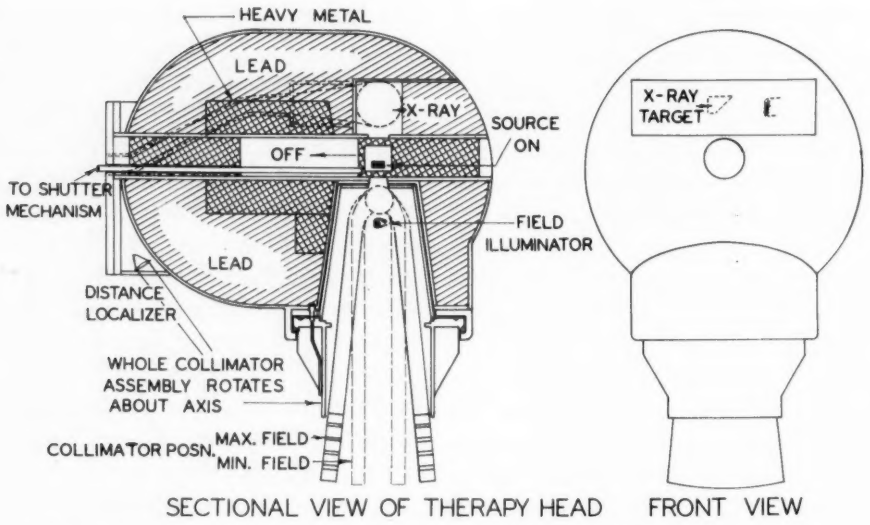


FIG. 2. Diagram showing the construction of the head of the cobalt unit.

metal slug 3 inches in diameter, holds the standard source as indicated. This heavy metal slug is moved along a horizontal line by a rod and a shutter mechanism mounted in the hollow steel column. To minimize the size of the head, some heavy metal is incorporated in the region immediately adjacent to the source. A conical opening in the head is coaxial with the beam and into this conical opening is placed a cone carrying the collimator. Behind the source in the "on" position is the roentgen-ray target. The collimator rotates about the axis of the beam and can be set to give a maximum field of 20×20 cm. and a minimum field of 4×4 cm. at 80 cm. The speed of rotation of the unit can be varied from 0 to 1 rpm. from the control panel or in the treatment room.

THE COLLIMATOR

The conical shaped opening shown in Figure 2 is arranged so that practically all of the space between the patient's skin and the source may be devoted to the collimator. The "on," "off" mechanism is completely independent of this and does not involve this space near the source. In an earlier paper[5] a collimator making use of a large number of sliding bars which move so that the leading edges are always in line with the edge of the source was described. The present collimator makes use of only four main plates which are connected together in pairs and arranged so that the leading edges are always on a straight line towards the edge of the source.

In Figure 3 is shown one of the plates of the collimator. Each consists of a double bearing near the source, a steel bar connected to a series of arcs, welded together and filled with lead. To construct this bar

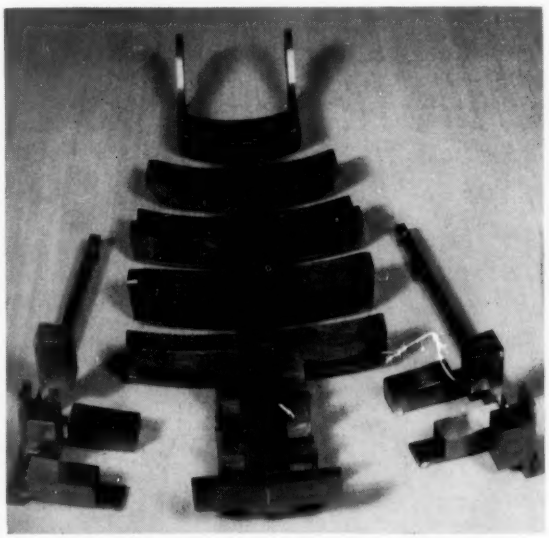


FIG. 3. Photograph of one of the plates of the collimator, of which there are four required. This photograph also shows the rectangular bars on the right and left hand side of the diagram, carrying two systems of heavy metal arcs at right angles.

the device was pivoted about an axis secured to the surface of the table top of a band saw and cuts made at the proper radius. The arcs should really be segments of the surface of a sphere, but for practical purposes may be cylindrical and so may be cut with a band saw using the correct radius with the table top of the saw set at the correct angle. The opposing pair of bars are essentially the same as those shown in Figure 3 except, where the arcs appear in this one, open gaps appear in the first one. It is to be noted that in the segment shown in Figure 3 there are five crescent shaped arcs

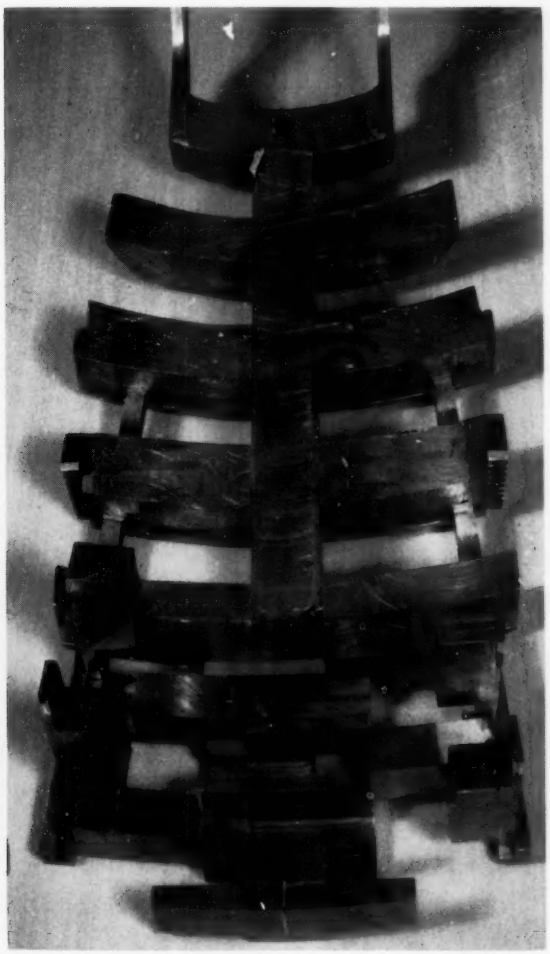


Fig. 4. Photograph of the same plate as in Figure 3 with the corner pieces mounted in the slots provided, and arranged in the open position. The corner pieces can be pushed to the center causing the heavy metal pieces to slide in the slots provided.

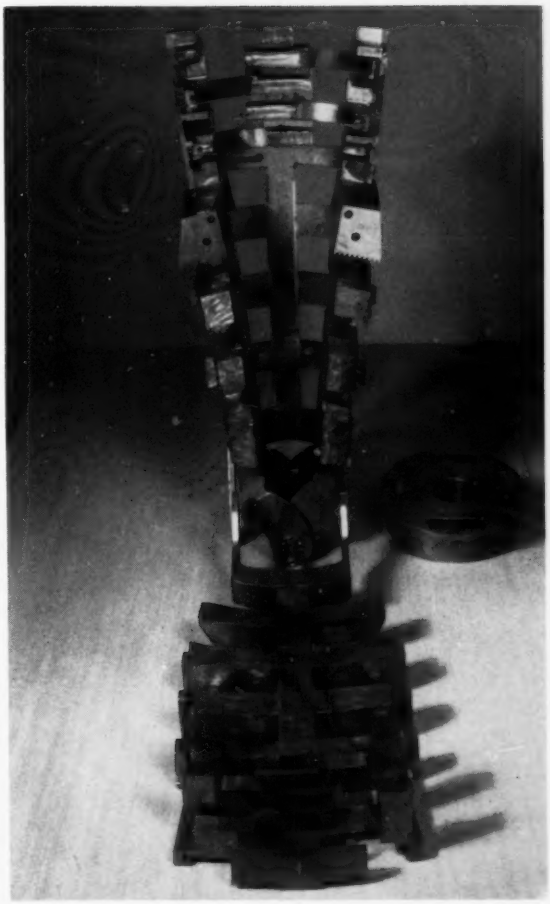


Fig. 5. Photograph showing the four plates: One lying flat on the table, the other ones mounted about their appropriate bearings. The piece of steel on the right hand side shows the four pivot points.

next to the source, while remote from the source the arcs are replaced by a series of curved shelves of length about half the arc lengths. Into the upper end of this plate are inserted the two corner bars, as indicated in Figures 3 and 4. When the corner pieces are pushed towards the center, the bars slide along the curved shelves. In Figure 5 is shown a photograph of the four main plates arranged artificially with one of them opened up, so that the assemblage of the other three may be seen. From this photograph it is obvious that when the one which is lying on the table is rotated through 90°, it will slide into the openings provided by the two vertical ones. In Figure 6 the four systems are shown assembled, with the two

FIG. 6. Photograph showing the four sets of plates mounted together and the four corner pieces in place. The whole assembly fits inside the cone on the left hand side.

sets of bearings at the axis being evident. Two sets of racks can be seen in Figure 6. These are part of the mechanism for opening and closing the collimator mechanism. This whole assembly shown in Figure 6 is mounted inside the cone on the left hand side of the diagram. A rectangular box-like arrangement is then mounted on top of the cone and carries the gear mechanisms for opening and closing the collimator. In Figure 7 are shown the cone, the box-like arrangement and the gear mechanism. On the left hand side appears a dial which is fastened to one gear which meshes with the other large gear. On the inside of the box are two small pinions which engage in curved rack gears which drive one plate to the right and the other to the left. The torque generated, on the left hand side of the photograph, is transmitted to the back side of the box through a gear and shaft which is shown in the bottom right hand corner of the square box of Figure 7. On the back of the box appear two other gears identical with the ones on the front, which are connected to two more pinions which engage the arcs at the back. Thus, each corner of the two pairs of segments are driven by a gear. This arrangement makes for great stability and prevents any distortion of the system. With the arrangement described, there are only four bearings at a point in space just below the source. The center of gravity of the system of two plates remains fixed in space as the mechanism opens and closes so that there is no difficulty in changing the field size for any orientation of the head.

In Figure 8 is shown a view of the collimator in the open position taken from a point along the axis looking towards the source. Figure 9 is a similar photograph, taken with one dimension closed, the other one wide open, giving a 20×4 cm. field.

It is interesting to compare this collimator with the one developed by Johns and McKay[5] making use of a large number of moving vanes sliding in such a way as to present a straight line drawn from the edge

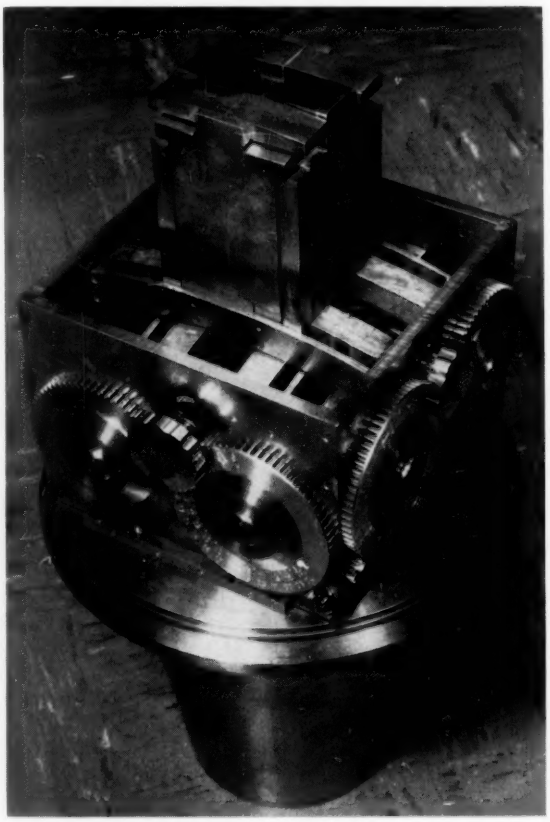


FIG. 7. Photograph showing the cone in place, the rectangular box mounted on top of the cone with the gear mechanism and the four plates in the inner position.

of the source. In the original collimator the protection was best with the system wide open and the outer dimensions of the device remained the same regardless of field size. In the device described here, protection is best when the collimator is closed, and the outer dimensions of the device increase with increase in field size.

Figure 10 shows a schematic diagram of the collimator construction. On the left hand side of the diagram, the cone is apparent and the position of the two sets of pivots at right angles to each other. One of the moving plates is shown cross-hatched. The position of the rack gears for adjusting this plate is shown. The lower end of the plate shows the shelves which carry the sections which are mounted on the corner pieces. The corner pieces are shown in the diagram as well. The protection afforded by the device is illustrated in section AA which shows the cross section at the level A. At the level B the protection is shown by the sectional view BB. This is the same as AA except it has been rotated through 90°. The protection at level C and B is shown by the sections CC and BB, for maximum field size. For ease in comparison the dotted lines of section CC and DD show the protection in the plane either above or below the one shown. It is apparent that complete protection is provided by adjacent layers, that is, the protection which is lost in one plane is gained in the next one. Finally, in section DD is shown the position of the bars in the closed position. Now a solid wall of heavy metal of $1\frac{1}{4}$ inches on each side provides the protection. Before leaving the construction of the collimator it should be pointed out that the four main segments are made of steel filled with lead, whereas the plates at the end and the corner section are made of heavy metal. With this particular design there are no sliding surfaces and friction is kept to a minimum.

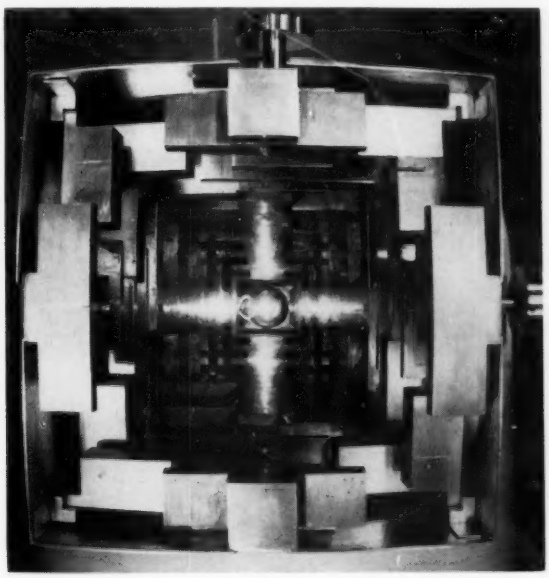


Fig. 8. Photograph taken from the end along the axis of the beam with the collimator in the open position.

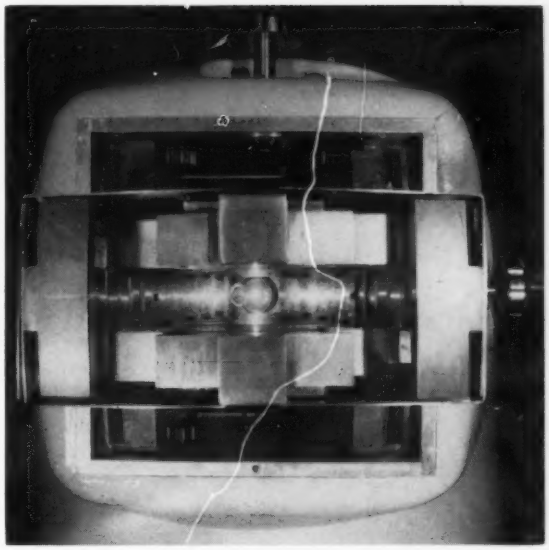


Fig. 9. Similar photograph as in Figure 8, with a field size set to 4×20 cm.

COUNTERWEIGHT

The construction of part of the counterweight is shown in Figure 11. The focussing lead plug and the ion chamber are shown in place. The focussing lead plug consists of a large number of holes 6 inches long pointing at an angle towards the source. This arrangement removes most of the scattered radiation from the patient and allows the ion chamber to "see" only primary radiation from the source attenuated by the patient. A measurement of the amount of radiation transmitted through

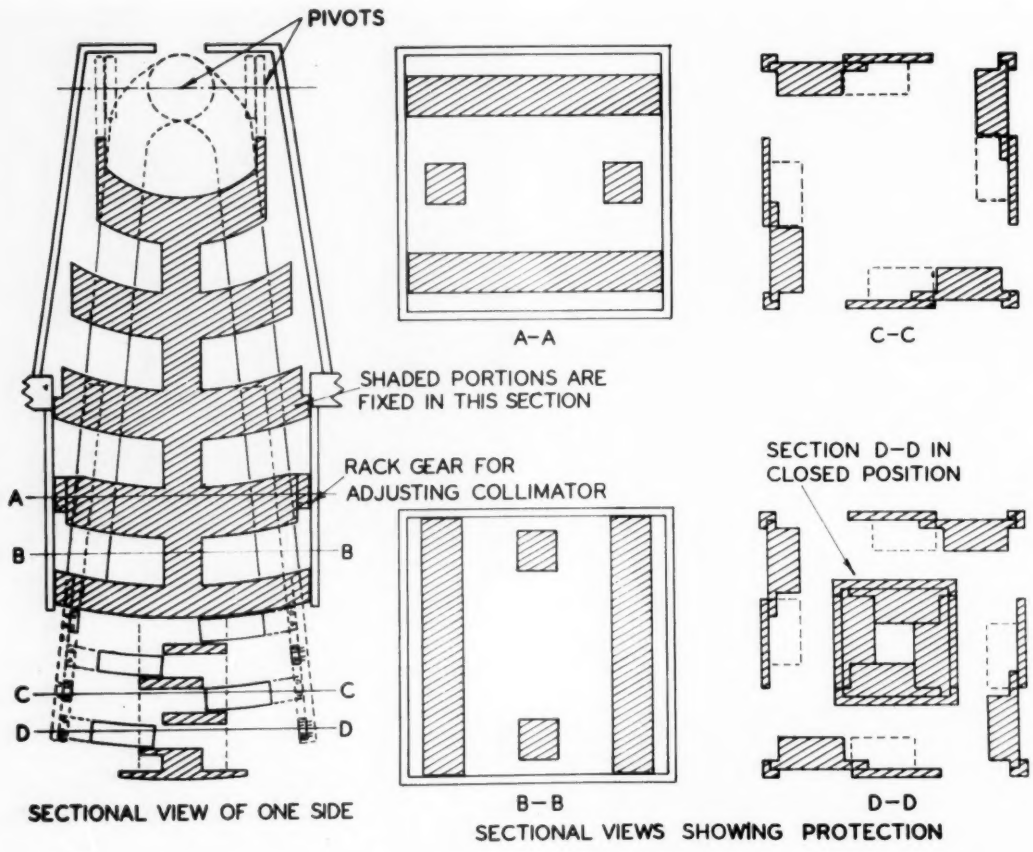
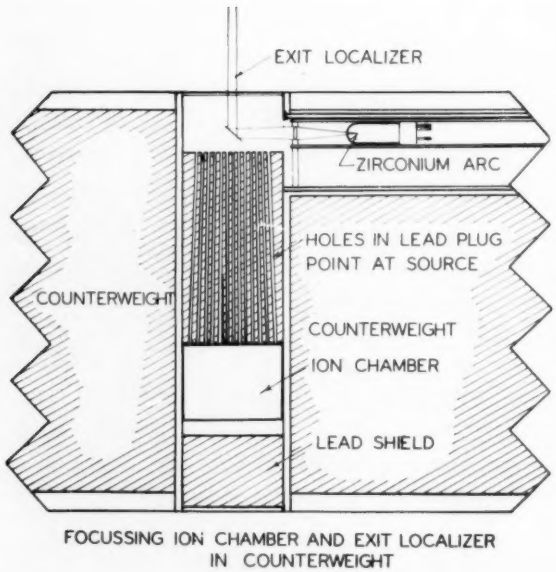


FIG. 10. Schematic cross sectional diagram of the collapsing collimator indicating the protection in the various planes.



the patient gives the radiographic thickness of the patient. No corrections need be made for scattering. The response of the ion chamber will be presented at the control panel on a recording potentiometer so that it will be possible to correct for air in the lungs, bone in the beam, etc. Details of this focussing lead plug and ion chamber have been published elsewhere.[3]

In Figure 12 is shown a photograph of the unit in place in the Ontario Cancer

FIG. 11. Diagram of the construction of the counterweight with the lead plug with its tapered openings mounted above the ion chamber. The exit localizer is indicated. This makes use of a zirconium arc, an acromatic lens which gives a very sharp bright spot on the axis of the beam and marks the exit point.

Institute with the head up and the floor level. On the right hand side can be seen the roentgen-ray control panel. The size of the collimator with respect to the counterweight, etc. can be judged from the nurse standing in the photograph. The treatment couch is not yet completed, but will be arranged so that it can be pivoted about a point on the axis of the beam.

In Figure 13 is shown a photograph of the head in the down position with the collapsing floor down to make room for the head. The collimator in this photograph is shown in the closed position.

Fig. 13. Photograph of the unit with the floor collapsed and the head below the floor as would be the case at one instant during rotation therapy.

THE CONTROL PANEL

The control panel for a cobalt 60 unit can be made very simple. In all of the treatment units to be installed in the Ontario Cancer Institute, use is being made of a type of integrator which enables us to carry out treatments without ever having to multiply or divide to get the correct treatment time. Details of the device will be found elsewhere.[1] The nurse selects the exposure dose in roentgens on one dial and the field size on a second dial. The machine is turned off after the prescribed dose for that particular field size has been administered. Corrections for the decay of the source may readily be made every month by moving one of the scales with respect to another.

Fig. 12. Photograph of the unit with the floor level as would be the case for fixed field therapy.

The unit has been in operation for four months and appears to be a practical precision unit for fixed field and rotation therapy.

SUMMARY

A new type of cobalt 60 unit has been constructed to be practical for both fixed field and rotation therapy. The penumbra has been kept small through the use of a special collimator and adequate source to tumor distance. Devices for accurate beam alignment including a roentgen-ray tube have been built into the head. A focussing ion chamber for transmission dose measurements is incorporated in the counterweight. Details of the unit are presented.

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The advice of Dr. C. L. Ash, Director of the

Institute, and the other members of the clinical staff in the development of this unit was appreciated.

REFERENCES

1. BAKER, R. G., WEBB, H. P., and JOHNS, H. E. Automatic dose computer for radiotherapy equipment. To be published.
2. BRAESTRUP, C. B., GREEN, D. T., and SNARR, J. L. Convergent beam irradiator; apparatus for convergent beam irradiation with stationary or moving sources. *Radiology*, 1953, *61*, 614–624.
3. FEDORUK, S. O., and JOHNS, H. E. Transmission dose, measurements for Co^{60} radiation with special references to rotation therapy. *Brit. J. Radiol.*, 1957, *30*, 190–195.
4. JOHNS, H. E., BATES, L. M., and WATSON, T. A. 1000 curie cobalt units for radiation therapy. I. The Saskatchewan cobalt 60 unit. *Brit. J. Radiol.*, 1952, *25*, 296–302.
5. JOHNS, H. E., and MACKAY, J. A. Collimating device for Co^{60} teletherapy units. *J. Fac. Radiologists*, 1954, *5*, 239–247.
6. JOHNS, H. E. Physical aspects of rotation therapy. AM. J. ROENTGENOL., RAD. THERAPY & NUCLEAR MED., 1958, *79*, 373–381.
7. KLIGERMAN, M. M., TAPLEY, N. DU V., and JACOB, G. Consideration of rotation therapy with 22.5 mev. betatron. AM. J. ROENTGENOL., RAD. THERAPY & NUCLEAR MED., 1958, *79*, 387–393.
8. MEREDITH, W. J. Some aspects of supervoltage radiation therapy. AM. J. ROENTGENOL., RAD. THERAPY & NUCLEAR MED., 1958, *79*, 57–63.

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PHYSICAL AND CLINICAL ADVANTAGES AND LIMITATIONS OF COBALT 60 TELETHERAPY*

PART I. PHYSICAL FACTORS

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THE basic advantages and limitations of cobalt 60 teletherapy are today well established, yet the practical significance of the differences between cobalt 60 and 250 kv. roentgen therapy deserves further evaluation. Only some of these differences will be considered in detail as the others have been discussed extensively in earlier reports.[1,3,4,5]

LEVEL OF MAXIMUM DOSE

The term cobalt 60 teletherapy, as used today, covers a wide range of techniques and too often it is assumed that they all fully utilize the advantages of high energy irradiation. Typical is the question of skin sparing effect. As a result of the high energy of the secondary electrons produced by the cobalt 60 gamma beam, the maximum ionization occurs about 0.5 cm. below the skin of the patient; with 250 kv. the maximum ionization is at the surface or in the cutaneous tissue. This advantage of cobalt 60, however, is achieved only if there is no significant electron contamination of the beam. That may be accomplished either by adequate distance, about 15 cm. between beam collimator and skin, or by the use of electron filters. Metals of intermediate atomic number, such as brass, are used for this purpose.[6] On the other hand, plastic-bottomed cones close to the patient will cause the maximum ionization to occur in the skin; they should, therefore, not be used where the skin sparing effect is important. With some techniques, such as rotation, the dose at the surface is often so low, however, that it is not significant whether the maximum level is at the skin or 0.5 cm. below. An approximate check for electron contamination may be made by comparing the readings obtained with the ordinary thin-walled thimble chamber before and after the cap has been added to establish electronic equilibrium. An increase of about 30 per cent with the cap on indicates that the beam contains mainly gamma rays. This is discussed in detail in an earlier report.[2]

DEPTH DOSE

Another advantage of cobalt 60 teletherapy is the higher depth dose. For cobalt 60, this factor is usually expressed in per cent of the maximum dose, that is, the value measured 0.5 cm. below the skin. Obviously, any comparison of depth doses must take into account the other factors affecting the depth dose, such as source-skin distance and field size. Figure 1 shows the percentage depth doses at 10 cm. depth and with a fixed field size of 10×10 cm. for 250 kv. and cobalt 60 radiation. It will be seen that for the same source-skin distance the depth dose is about 40 per cent higher with cobalt 60. The chart shows, also, that in order to get the same percentage depth dose with roentgen rays as obtained with cobalt 60 at 25 cm. source-skin distance, the target-skin distance has to be about 65 cm.

The actual gain by using cobalt 60 is usually not as great as indicated since the exit dose is also higher, a factor which must be considered when using opposing fields. This is illustrated in Figure 2 which shows the same comparison for cross-firing through a 20 cm. thick patient. For the same source distance, the increase in tumor dose with cobalt 60 is only 30 per cent for the same "skin" dose.

So far we have considered only a 10×10

* From the Department of Radiology, College of Physicians and Surgeons, Columbia University and Francis Delafield Hospital, New York, New York. Presented at the Fortieth Annual Meeting of the American Radium Society, Hollywood, Florida, March 27–29, 1958.

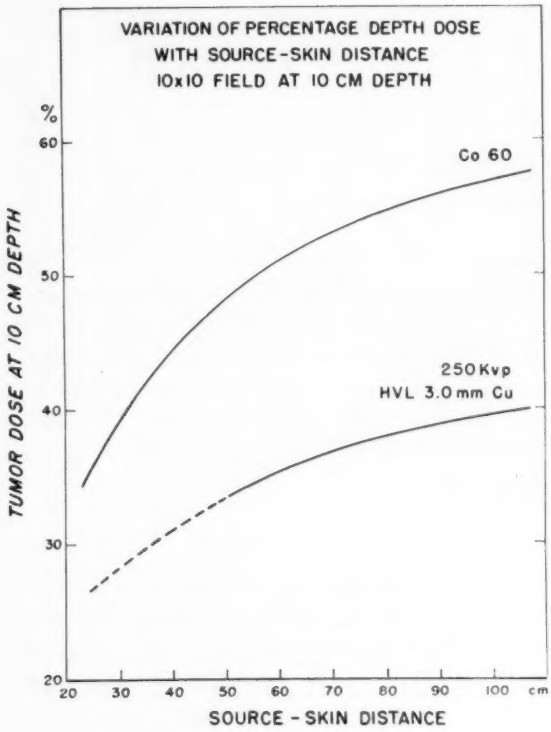

FIG. 1. Comparison of depth dose.

cm. field. As shown in Figure 3, the difference in depth dose is less pronounced for the larger fields. This, of course, may be expected as the higher energy rays of cobalt 60 are scattered mainly in the forward direction. It should be emphasized that the percentage depth dose is only one of the physical factors to be considered in treatment planning. It is particularly important to bear this in mind with cobalt 60 teletherapy, and especially when using rotation. Usually, it is no longer the skin tolerance which is the limiting factor in giving a cancerocidal dose to deep-seated tumors but rather the dose received by vital organs near the tumor. It is essential, therefore, to determine the complete isodose pattern around the tumor volume.

OTHER ADVANTAGES OF COBALT 60

One of the principal gains of using cobalt 60 teletherapy is the reduced integral dose. This has already been emphasized in a paper presented in 1957 before the American Radium Society by Maus and McCormick.[4]

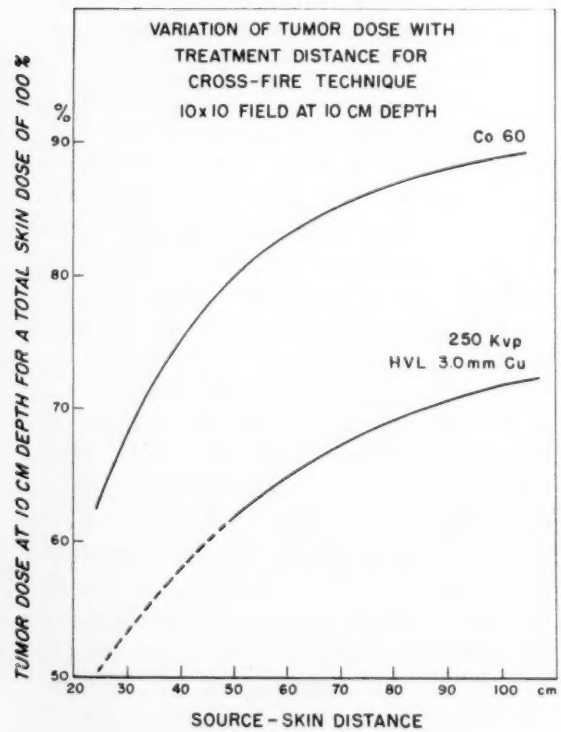
VARIATION OF TUMOR DOSE WITH
TREATMENT DISTANCE FOR
CROSS-FIRE TECHNIQUE
10x10 FIELD AT 10 CM DEPTH
%
Co 60
250 Kvp
HVL 3.0 mm Cu
TUMOR DOSE AT 10 CM DEPTH FOR A TOTAL SKIN DOSE OF 100 %
SOURCE - SKIN DISTANCE
cm

FIG. 2. Comparison of tumor dose.

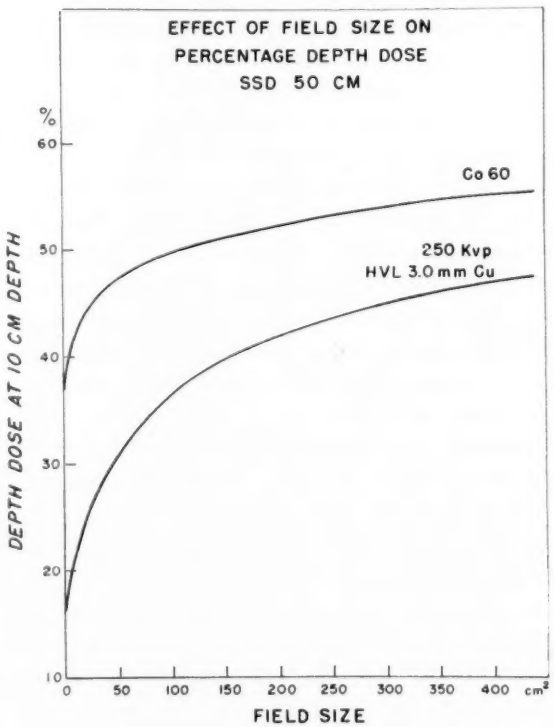

FIG. 3. Effect of field size on percentage depth dose.

The reduced relative absorption in bone compared with soft tissue for cobalt 60 has also been stressed in previous reports.[5,7] The compactness of the cobalt 60 source and its housing permits it to be rotated around the recumbent patient with the useful beam always directed at the tumor volume. This type of equipment has the advantages of better fixation and greater comfort to the patient than if he were rotating and the beam were stationary.

To these advantages of cobalt 60 should be added the nonfluctuating output and the high degree of homogeneity of the gamma radiation. Both factors permit more accurate radiation measurements and dose determinations. Once the r/min. has been established there is no need for frequent recalibrations; furthermore, the half-value layer or energy of the beam is essentially the same for all cobalt 60 teletherapy machines.

The output of roentgen-ray equipment is subject to considerable variation. This may be caused by line voltage fluctuation, heating-up of the equipment and erratic behavior of roentgen-ray and valve tubes. Where no radiation monitor and voltage adjustment are used, the variation in r/min. may well exceed 10 per cent and is, therefore, of clinical significance. Another disadvantage of roentgen ray equipment is the unpredictable life expectancy of the roentgen-ray and valve tubes. This is of particular importance in clinics where there is just one therapy machine and where no nearby repair service is available. A breakdown may thus cause prolonged interruption of treatments. The replacement of the cobalt 60 source, on the other hand, can be scheduled in advance so as to cause minimum inconveniences. Cobalt 60 equipment requires no observation of meters nor manipulation during operation. This gives the technician more time to watch the patient.

PENUMBRA

Until recently, two principal limitations of cobalt 60 teletherapy were significant: penumbra and low radiation output. The problem of penumbra was discussed by several speakers at the 1957 meeting of the American Radium Society; all agreed that penumbra is undesirable. This writer, too, regards excessive penumbra objectionable but believes that the method of reducing it deserves further consideration.

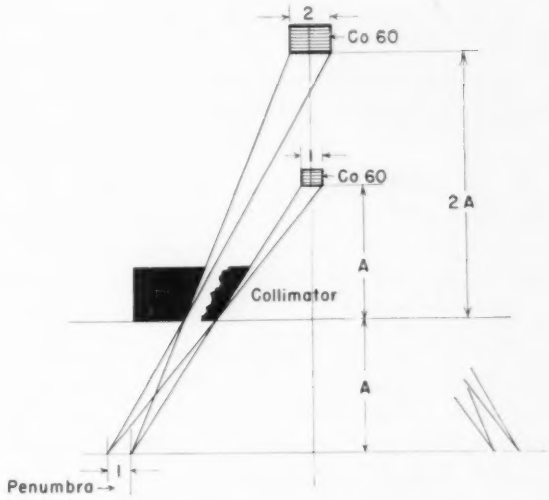

Fig. 4. Effect of distance and source diameter on penumbra.

The size of the penumbra at the tumor is determined by just two factors: the dimensions of the source and the ratio of the collimator-tumor distance to the collimator-source distance. The product of these two factors determines the geometric penumbra irrespective of collimator design. Figure 4 illustrates the two methods by which the penumbra can be reduced. One is to reduce the size of the source; the other, to increase the source-tumor distance and retain the same collimator-tumor distance. In the earlier days of cobalt 60 teletherapy, most therapeutic sources had large diameters, 3 cm. or more. Due to the production of cobalt 60 of high specific activity, it is possible today to obtain kilocurie sources as small as 1.5 cm. in diameter. The average 250 kv. roentgen-ray tube has a focal spot of about 1.0 cm.

In Table 1 is shown the relationship between source-tumor distance and source size for a fixed penumbra of 1 cm., an exposure rate of 40 r per minute in air at the

TABLE I

GEOMETRIC PENUMBRA 1.0 CM., 40 R/MIN. AT TUMOR (AIR), COLLIMATOR-TUMOR DISTANCE 25 CM., FIELD 10×10 CM. AT 10 CM. DEPTH

Source-Tumor Distance, cm.	Source Diameter, cm.	r/min. at 1 m.	Curies Approx.	Per Cent Depth Dose at 10 cm.
37.5	0.5	5.6	340	37.8
50	1.0	10.0	600	44.5
75	2.0	22.5	1350	52.1
100	3.0	40.0	2400	56.1

tumor, and a collimator-tumor distance of 25 cm. A shorter collimator-tumor distance may be used with stationary fields if the cone is provided with an electron filter. For rotation, it is desirable that the collimator-tumor, or collimator-axis, distance be at least 30 cm. to minimize the possibility of collision. It is obvious that if penumbra were the only consideration, a small diameter source used at a relatively short treatment distance would be the most advantageous. The greater distance still offers the advantages of a higher depth dose and larger fields where that is required.

In Table II is shown the relationship between geometric penumbra and distance for a 2 cm. diameter source. Obviously, there is no technical difficulty in reducing the penumbra to any desired value by increasing the source-collimator distance. With the greater distance, however, it is necessary to use a larger source to maintain the same dose rate at the tumor. The question naturally arises whether a reduction in the penumbra of a few millimeters is worth the additional expense of several thousand dollars. There is not merely the higher cost of the source to be considered but also the greatly increased weight and expense of equipment and room shielding. In most cases it would appear that reducing the geometric penumbra below 1 or 2 cm. is justified only if the extent of the lesion is known within those limits. A penumbra of that order of magnitude does not add significantly to the integral dose. The increase is generally less than that due to incomplete collimation, such as caused by irradiation of irregularly shaped tumors through rectangular fields.

So far, we have considered only the geometric penumbra. In addition to the geometric penumbra, there is also the transmission penumbra; that is, the penumbra caused by the incomplete attenuation of the rays by the edges of the collimating system. This is illustrated in Figure 5. The transmission penumbra can be minimized by constructing the diaphragms of high atomic number materials, such as tungsten alloys or, still better, uranium. It can be reduced also by having the edge of the collimator directed at the edge of the source.

OTHER CONSIDERATIONS

Cobalt 60 sources are available today with radiation outputs exceeding 250 kv. roentgen-ray equipment; the principal limitation is cost. While the price of cobalt 60 is less than one third of what it was four years ago, the present source replacement cost

TABLE II

SOURCE DIAMETER 2.0 CM., 40 R/MIN. AT TUMOR (AIR), COLLIMATOR-TUMOR DISTANCE 25 CM., FIELD 10×10 CM. AT 10 CM. DEPTH

Source-Tumor Distance, cm.	Geometric Penumbra, cm.	r/min. at 1 m.	Curies Approx.	Per Cent Depth Dose at 10 cm.	Cost* Approx.
37.5	4.0	5.63	340	37.8	$ 1,250
50	2.0	10.0	600	44.5	2,275
75	1.0	22.5	1350	52.1	5,500
100	0.67	40.0	2400	56.1	10,600
125	0.50	62.5	3750	58.2	17,700

* Does not include cost of loading, calibration and shipping.

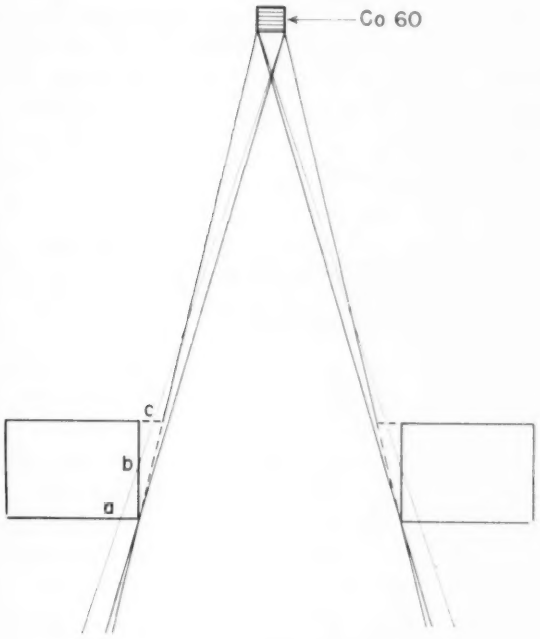

FIG. 5. Transmission penumbra.

usually exceeds the maintenance expense of roentgen-ray equipment. The initial output of the source must be sufficient to take care of the expected patient load several years later, until it is replaced. In order not to have too frequent source replacements, the initial output should preferably be about twice the minimum required. This permits the source to be used for about five years before its replacement.

The cost and weight of cobalt 60 teletherapy equipment varies widely depending upon the output, degree of flexibility and whether or not rotation is available. In general, 250 kv. roentgen-ray apparatus is somewhat less expensive and lighter than cobalt 60 kilocurie apparatus. Of even greater importance is the difference in the room shielding requirements. Frequently, weight considerations alone determine the feasibility of installing cobalt 60 teletherapy equipment on upper floors of existing buildings. This is illustrated in Figure 6. It will be seen that the primary concrete shielding has to be about two and one-half times thicker for cobalt 60. The primary barrier thickness may be reduced by incorporating a shield in the equipment or eliminated entirely by locating the equipment in the basement and directing the useful beam toward earth-backed barriers only. The drawing illustrates, also, the rela-

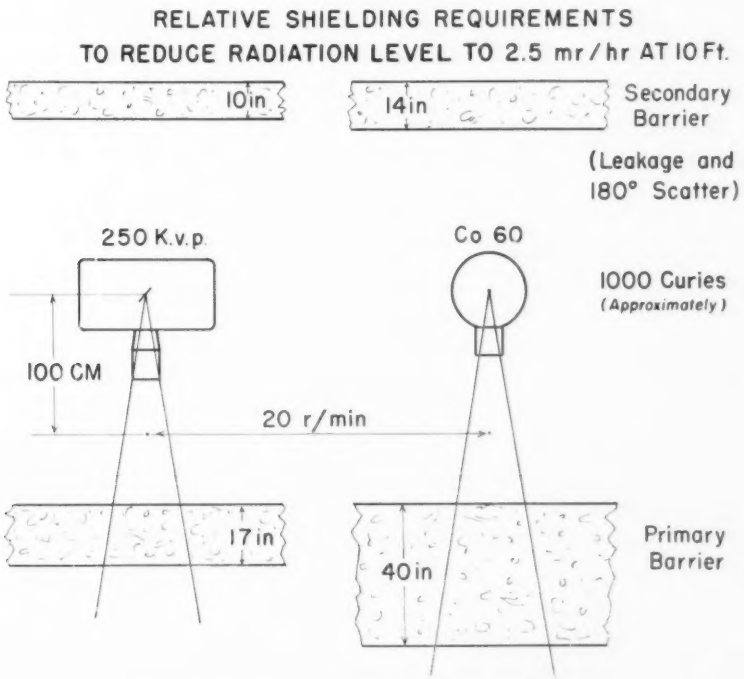

FIG. 6. Comparison of shielding requirements.

tive secondary shielding requirements. The difference is less, especially for barriers exposed to radiation scattered through a large angle. For 180 degree scatter, the difference is relatively small. For 45 degrees, the barrier for cobalt 60 radiation has to be about twice that for 250 kv. roentgen rays.

So far, only the physical factors relating to irradiation of deep-seated tumors have been considered. Most clinics must also be able to treat lesions located only a few centimeters below the skin. This presents no difficulty with roentgen-ray equipment as the depth dose can readily be reduced by using lower voltage and less filtration. With cobalt 60 teletherapy, reduction in depth dose is accomplished only by using a shorter source-skin distance; the minimum possible distance will depend on the construction of the equipment. It may, therefore, not be feasible to reduce the depth dose sufficiently. This problem often arises when replacing the only 200 or 250 kv. roentgen-ray machine of a department with cobalt 60 teletherapy apparatus. In such cases, the addition of a 135 kv. roentgen-ray machine often provides the logical solution as it can be used for both skin and intermediate roentgen therapy.

SUMMARY

It has been shown that cobalt 60 teletherapy offers significant advantages over 250 kv. roentgen rays in the treatment of deep-seated lesions. Earlier limitations of very pronounced penumbra and low output have been eliminated by the availability of high specific activity sources. Cobalt 60 teletherapy still has the inherent disadvantages associated with high energy irradiation; that is, the higher cost and greater shielding requirements.

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REFERENCES

1. BRAESTRUP, C. B., and MOONEY, R. T. Physical aspects of rotating telecobalt equipment. *Radiology*, 1955, *64*, 17–27.
2. BRAESTRUP, C. B. and MOONEY, R. T. Cobalt 60 radiation measurements. *Radiology*, 1958, *70*, 516–522.
3. JOHNS, H. E., Physical aspects of rotation therapy. AM. J. ROENTGENOL., RAD. THERAPY & NUCLEAR MED., 1958, *79*, 373–381.
4. MAUS, J. H. and MCCORMICK, N. A. Three years' clinical experience with rotation therapy with the theratron. AM. J. ROENTGENOL., RAD. THERAPY & NUCLEAR MED., 1958, *79*, 382–386.
5. MEREDITH, W. J. Some aspects of supervoltage radiation therapy. AM. J. ROENTGENOL., RAD. THERAPY & NUCLEAR MED., 1958, *79*, 57–63.
6. RICHARDSON, J. E., KERMAN, H. D., and BRUCER, M. Skin dose from a cobalt 60 teletherapy unit. *Radiology*, 1954, *63*, 25–36.
7. SPIERS, F. W. Influence of energy absorption and electron range on dosage in irradiated bone. *Brit. J. Radiol.*, 1949, *22*, 521–533.

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PHYSICAL AND CLINICAL ADVANTAGES AND LIMITATIONS OF COBALT 60 TELETHERAPY*

PART II. CLINICAL CONSIDERATIONS

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DURING the past few years several papers have been published which dealt with the advantages and limitations of supervoltage radiation therapy. It is interesting to note that all the authors expressed the opinion that treatment with 1–4 mev. units would bring about improvement of existing results only if the superior physical qualities of these machines could be effectively utilized, as the biologic effect on cells is essentially not different from that achieved with 250 kv. machines. These physical factors are: maximum ionization at 0.5 cm. below the surface, good penetration, diminished scatter and decreased absorption of radiation in bones and cartilage. They make possible the delivery of a high dose to the depth without undue impairment of skin or other overlying structures, improve the general tolerance of the patient and prevent or, at least, alleviate the undesirable drop in the blood count. Obviously, supervoltage radiation therapy is best suited for the treatment of deep-seated lesions or of extensive disease where a large volume is included in the field of irradiation.

These well known facts have been established for quite some time, and I do not believe that anything new can be added. The machines have been standardized; isodose curves have been plotted and are being constantly used for treatment planning. A change has occurred, however, with the introduction of different cobalt 60 models which, while alike in name, are not necessarily alike in performance.

The purpose of this paper is to call attention to these variations, and to emphasize the necessity of their full understanding, although it is not intended to weigh advantages and disadvantages of different cobalt 60 units against each other. A need for correction of certain misconceptions exists and examples of treatment plans of lesions of the neck, thorax and pelvis may help to illustrate this point. For instance, let us assume the aim is to deliver to a lesion in each of these three locations a tumor dose of 5,000 r in five weeks time through fields of three different sizes: 5×5 cm., 12×12 cm. and 15×15 cm.

NECK

In the case of the neck, a lesion of the larynx usually is situated 5 cm. from the surface. Obviously, a tumor which is so close to the surface does not need to be treated with supervoltage radiation; high voltage roentgen therapy will produce the desired result.

Figure 1 demonstrates the approach with a 250 kv. unit with a half-value layer of 3 mm. Cu at a 50 cm. target-skin distance. For a tumor dose of 100 r, the skin dose at each of the opposing fields is 108 r, and for a total tumor dose of 5,000 r, the skin dose is 5,400 r, which is compatible with the survival of skin and underlying tissues for such a small area. When we superimpose on the isodose curves of a 250 kv. unit the isodose curves of a cobalt 60 unit with a half-value layer of 11 mm. of Pb operating at a source-skin distance of 25 cm., it becomes evident that the readings in the tumor and on the skin are essentially the same with

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Presented at the Fortieth Annual Meeting of the American Radium Society, Hollywood, Florida, March 27–29, 1958.

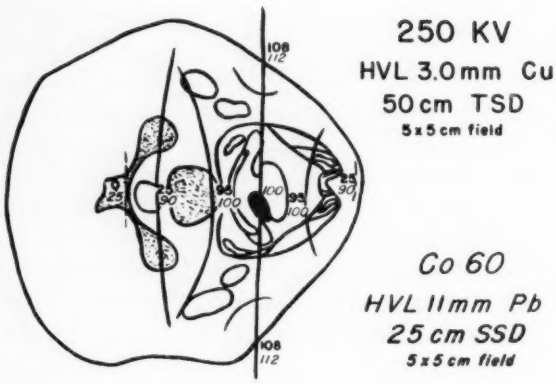

FIG. 1.

both sets of curves. The term skin applies in the case of a cobalt 60 unit to the point of maximum ionization at 0.5 cm. below the surface. For 100 r in the tumor the skin receives 112 r, and for a total tumor dose of 5,000 r the skin dose is 5,600 r, a dose which can well be tolerated. There are, however, important differences when one studies the readings beyond these two points of interest, owing to the differences in target-skin distance or source-skin distance. With the use of the 250 kv. unit, a point 1 cm. outside of the 5×5 cm. field receives 25 r for 100 r in the center of the tumor, or 1,250 r for the total tumor dose of 5,000 r. This is due to the penumbra effect. With the cobalt 60 source operating at 25 cm. source-skin distance, the dose on this identical point is approximately 90 r for 100 r tumor dose; in other words, an area 1 cm. outside of the intended field of radiation receives a total dose of approximately 4,500 r for the total tumor dose of 5,000 r. The area which receives this high dose unnecessarily would be, in this case, the spinal cord. These high readings are due to an increase in the field size at the depth when cobalt 60 sources are used at such short distances. In addition to this increase in the field size, the penumbra also has an effect on the irradiated area by widening it even further. At a point 5 cm. from the center of the field, a dose of approximately 25 r is received for 100 r at the center which means a total dose of 1,250 r to this point. It is, therefore, imperative to decrease the field size on the skin under the above described condition. When cobalt 60 units are used at source tumor distances of 55 to 75 cm., no appreciable difference exists between the field size on the skin and at a depth of 5 cm. The reason why supervoltage radiation therapy is suggested at all for lesions so close to the surface lies in certain advantages to the patient, especially as regards the better tolerance of the skin and cartilage. There is a definite and demonstrable difference in the permanent skin changes (Fig. 2 and 3) although the daily dose rate is the same and the total tumor dose and the field size are equal.

THORAX

In the case of the thorax, as, for example, when treating an inoperable carcinoma of the lung, the problems and procedures are quite different. It was observed at the Francis Delafield Hospital, New York City, that tumor doses of 5,000 r delivered in five

FIG. 2. Photograph of the skin of a patient taken three years after 250 kv. therapy showing telangiectasis and fibrosis.

weeks time produce beneficial results in an appreciable number of patients. The treatment approach in patients with peripheral lung lesions is through opposing fields. A dose of 5,000 r causes complete fibrosis in the treated lung, eliminating future function. Considering this fact, every effort is made to save the remaining lung, as the survival of the patient does not only depend on the elimination of the disease but also on the proper function of this normal lung.

Figure 4 demonstrates the treatment plan of a patient who was treated for a peripheral lung lesion with the theratron unit. This unit has a 1,500 curie cobalt 60 source of 2 cm. in diameter and is operated at a 75 cm. distance. For a tumor dose of 100 r to the center of the tumor, 10.4 cm. from the surface, the skin receives a dose of 119 r. For the total tumor dose of 5,000 r the skin dose is 5,950 r, a dose which does not cause much immediate skin reaction and does not produce late skin changes. The lateral margins of the field show a decrease of the dose, it being 90 r at 4.5 cm. and 60 r at 6 cm. from the center of the field. This, of course, is an important observation which may call for a correction when one is interested in the dose at the center and at the margin of the field being the same. The other important finding is the considerable dose outside of the field of irradiation due to a rather large penumbra, resulting in doses from 50 to 20 r over a 2.5 cm. range outside of the field. In the case of an inoperable carcinoma of the lung, the mediastinum unnecessarily receives 20 to 50 per cent of the central tumor dose. The penumbra of cobalt 60 units changes with the size of the source and with the distance. The larger the source, the larger the penumbra; the longer the distance, the larger the penumbra. Superimposed on this plan for 75 cm. source tumor distance are isodose curves of a cobalt 60 unit operating at 55 cm. distance. The basic isodose pattern is the same as far as the center dose and fall-off are concerned, but the difference between the skin dose and the tumor dose is slightly greater. A tumor dose of 5,000 r results in a skin dose of 6,500 r, which is a high dose even with the better tolerance to this harder beam of radiation. Although in most patients it is possible to carry out the ideal treatment plan and to deliver the desired tumor dose through opposing fields, it may occasionally become necessary to add another field because the patient's skin may not tolerate this amount of radiation.

Cobalt 60 units operating at a source-

Fig. 3. Photograph taken three years after cobalt 60 therapy showing the skin to be soft and without permanent changes.

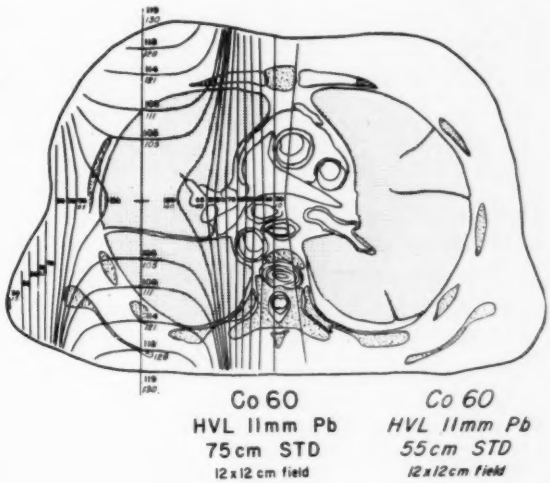

Fig. 4.

TABLE I

Type of Radiation	TSD or SSD	Field Size	At Skin	TTD or STD	Field Size	At Center
	cm.	cm.	cm.^{2}	cm.	cm.	cm.^{2}
250 kv., 3 mm. Cu	50	10×10	100	60.4	12.1×12.1	146
Co^{60}, 11 mm. Pb	25	10×10	100	35.4	14.2×14.2	200
Co^{60}, 11 mm. Pb	44.6	10×10	100	55	12.1×12.1	146
Co^{60}, 11 mm. Pb	64.6	10×10	100	75	11.7×11.7	144

skin distance of 25 cm. present an additional problem, as previously discussed (Table 1). As may be seen, the field size at 10 cm. depth increases greatly with a 25 cm. source-skin distance which makes a reduction of the field size at the skin level mandatory when cobalt 60 units with short source-skin distances are used in the treatment of deep-seated lesions. The penumbra with this cobalt 60 source is 1 cm. outside of the field. We have not been able to get a complete set of isodose curves for this unit, but we had it constructed by mathematical calculation. For a tumor dose of 100 r at the center, the skin gets 160 r, for 5,000 r at the tumor the skin receives 8,000 r. These readings are practically the same as those obtained from the 250 kv. unit (Fig. 5). To this high skin dose has to be added for the cobalt 60 unit, operating at a source-skin distance of 25 cm., the contribution due to electron contamination of the beam caused by the short distance between the collimator and the skin. It is generally accepted that the treatment of a deep-seated lung lesion with a 250 kv. roentgen-ray apparatus requires an approach through multiple fields and that for this reason the 250 kv. unit is not the most desirable machine for the treatment of this type of lesion; however, cobalt 60 units operating at short distances have the same shortcomings.

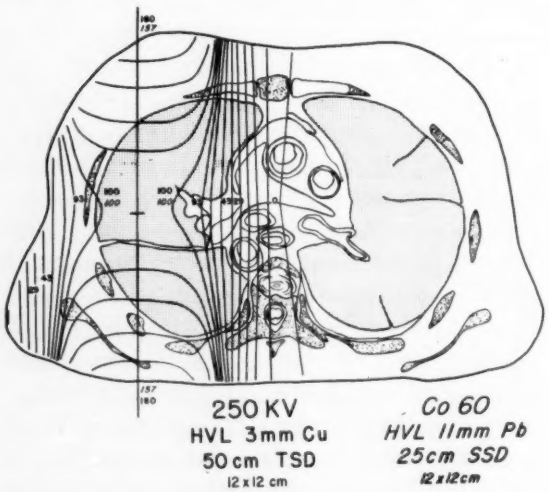

FIG. 5.

PELVIS

Finally, in the case of the pelvis, as, for example, a carcinoma of the cervix, a unique problem confronts us. I am referring to the necessity of delivering a sufficiently high dose to the lateral pelvic walls.

Figure 6 illustrates the treatment plan with a cobalt 60 unit operating at a distance of 75 cm. The treatment is directed through 2 opposing fields, measuring 15 ×15 cm. The proportion of tumor dose to skin dose is again favorable; it is 100 r at the center of the tumor and 119 r at the skin. However, on the lateral pelvic wall, we get only 72 per cent of the desired tu-

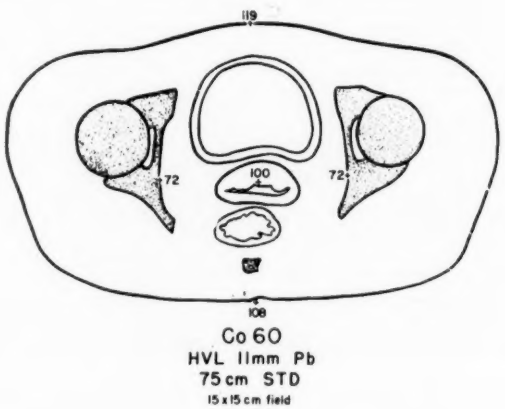

FIG. 6.

mor dose from 5,000 r, namely, 3,600 r. This we can remedy by using full rotation, if we treat carcinoma of the cervix with the cobalt 60 unit at all. The disadvantages of cobalt 60 units operated at shorter distances in treating this lesion are the same as have been discussed above in the treatment of thoracic lesions; *i.e.*, the increase in the field size at the depth, the unfavorable proportion between tumor dose and skin dose and the fall-off at the margin of the fields.

CONCLUSION

Cobalt 60 units are in a special group among the supervoltage radiation therapy machines because of the varying strengths of their sources which necessitate different distances. Exact knowledge of the inherent characteristics of the different cobalt 60 units is necessary to obtain the best possible results. These characteristics cannot be fully appreciated and understood unless isodose curves are used for treatment planning. Midline readings inform us only about the dose in the center of the field but do not give information about any other point of interest.

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A METHOD FOR CONSTRUCTION OF ISODOSE CHARTS FROM MINIMUM EXPERIMENTAL DATA*

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THE effective use of radiation therapy equipment requires certain basic physical information of which isodose distributions form an important part. A certain amount of this information is already published,[2] but where the conditions of use of the equipment are new, the distributions must be determined either by measurement or calculated by some of the accepted methods.[3,7,8,10] Particularly, where the apparatus to be used has multi-leaf diaphragm systems giving an infinite variety of field sizes, the amount of measurement or calculation involved is considerable.

The method described here permits the rapid construction of isodose curves from a very small number of measurements, and does not involve any calculation but simply the reading of information from graphical data. The system was developed during the calibration of a 700 curie cobalt 60 unit, the data from which are used to illustrate the method, but it is applicable to any quality of radiation and has been employed by the author for work at a half-value layer of 2.5 mm. copper and at 4 mev.

Three central plane isodose curves, namely 5×5 cm., 10×10 cm. and 15×15 cm. at 55 cm. source skin distance, were measured using a water phantom. The distances from the central axis, at which particular percentage depth dose values occurred, were read from these distributions at various depths and the values plotted against the square field axis size as shown in Figures 1 to 5. Obviously, the number of depths plotted depends on requirements. This family of graphs will be referred to as "square field isodose crossplots for 55 cm. source skin distance." Where the isodose contours are of such a shape as to permit, further points may be obtained by plotting from the measured distributions the distance from the central axis over which the isodose curves remain parallel to the incident surface. Such a curve for a Co^{60} unit is shown in Figure 6. The variation of central axis depth dose with source skin distance

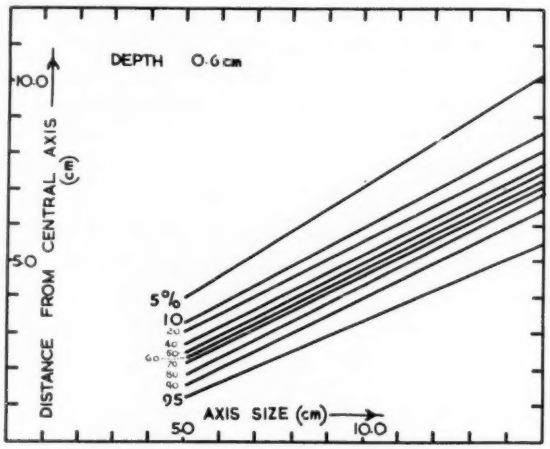

FIG. 1. Co^{60} square field isodose crossplots for 55 cm. source skin distance. Depth 0.6 cm.

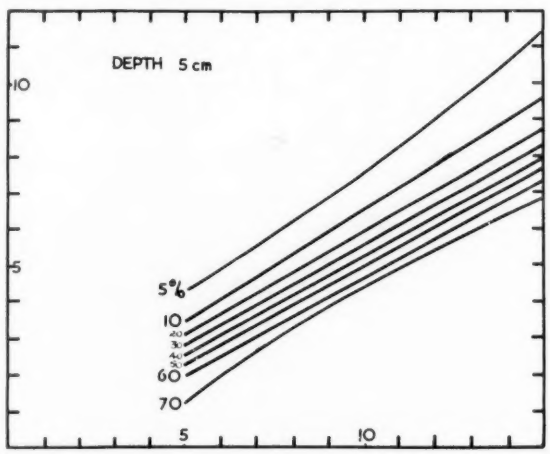

FIG. 2. Co^{60} square field isodose crossplots for 55 cm. source skin distance. Depth 5 cm.

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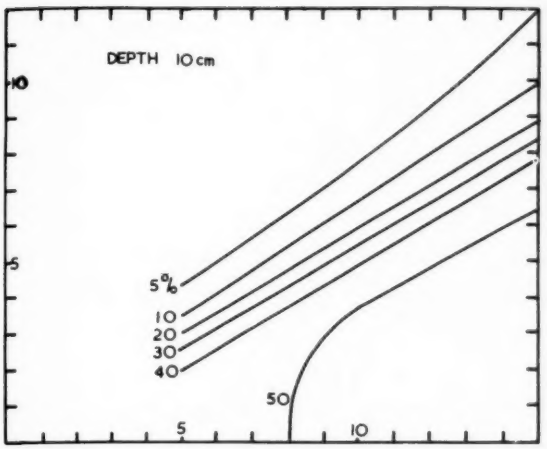

Fig. 3. Co^{60} square field isodose crossplots for 55 cm. source skin distance. Depth 10 cm.

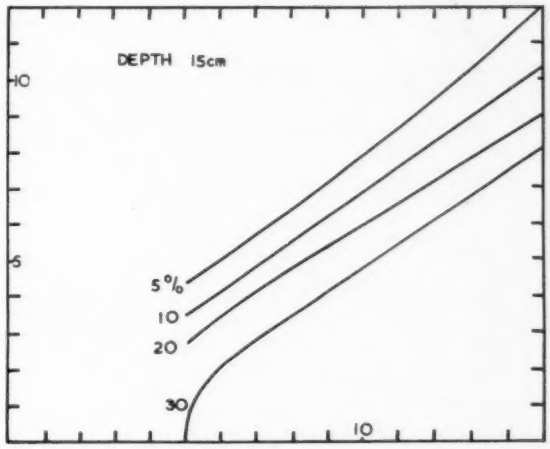

Fig. 4. Co^{60} square field isodose crossplots for 55 cm. source skin distance. Depth 15 cm.

was found to be in agreement with the F-factor (Mayneord and Lamerton, 1941).[6] The data of the *British Journal of Radiology*,[1] Supplement Number 5, together with the F-factor and the family of curves shown in Figures 1 to 5, enable us to construct complete isodose curves for any set of conditions. It was found that the F-factor variations led to the condition that the change in depth of a given central axis depth dose value was constant for all areas, and the data have been plotted in this way in Figure 7, normalized to a source skin distance of 55 cm. These data will be referred to as "depth corrections for source skin distances other than 55 cm." Using the above information it is possible to construct isodose distributions for a wide range of field sizes and source skin distances.

The steps in calculation are as follows.

A. *Square Fields.* (*a*) *At the normalized source skin distance* (in this case 55 cm.). Assuming that we wish to obtain the distribution for 7×7 cm. field we proceed as follows: the central axis depth dose values are plotted from the data in the *British Journal of Radiology*[1] and the positions relative to the central axis of the various percentage depth doses determined from the data of Figures 1 to 5. (*b*) *At other than the normalized source skin distance.* The central axis depth dose data at the normalized source skin distance are corrected using the infor-

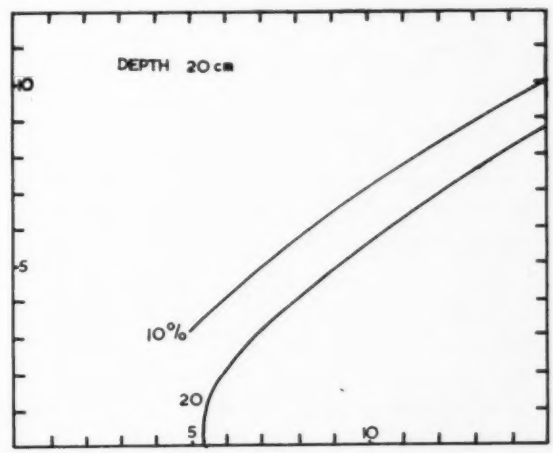

Fig. 5. Co^{60} square field isodose crossplots for 55 cm. source skin distance. Depth 20 cm.

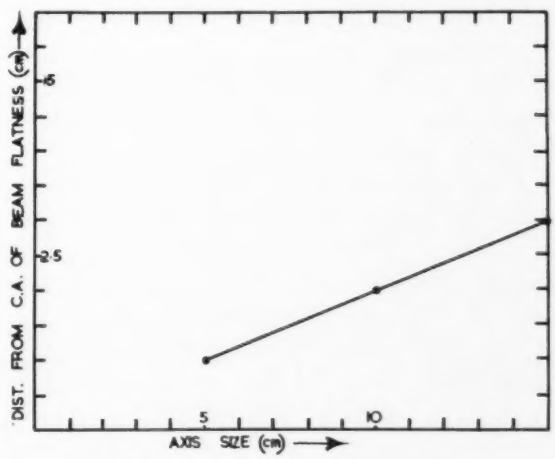

Fig. 6. Co^{60} square field beam flatness (applies to all depths beyond d_2).

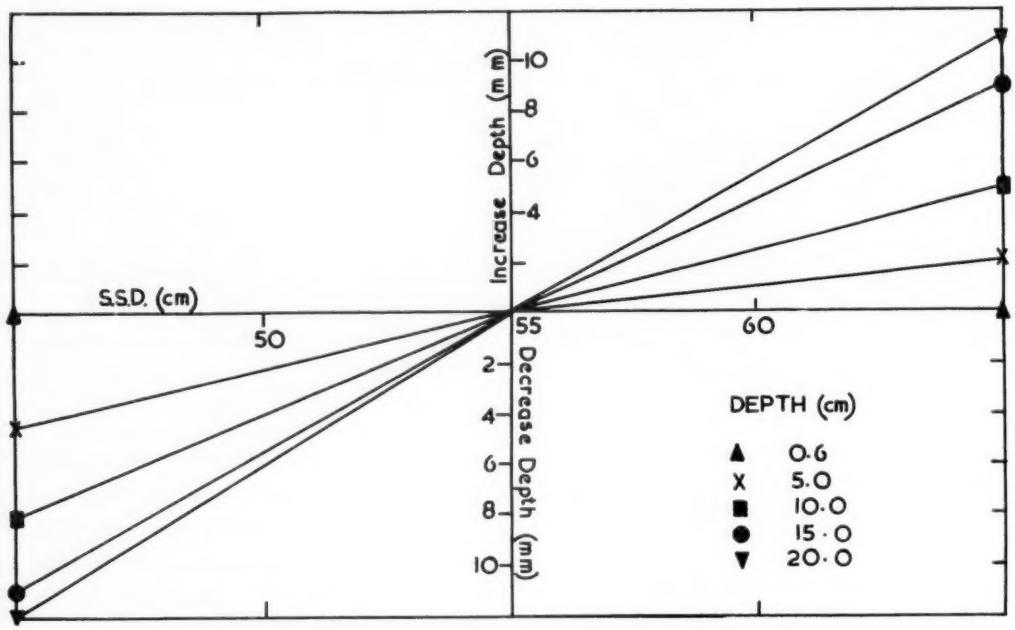

FIG. 7. Co^{60} depth corrections for source skin distances other than 55 cm.

mation in Figure 7. The same correction in depth is applied to the results obtained from the information in Figures 1 to 5. For example, at a source skin distance of 65 cm. the depth correction at a depth of 10 cm. amounts to 5 mm. From Figure 3 it will be found that at a depth of 10 cm. the position of the 10 per cent contour for a 7 cm. axis size is 4.8 cm. from the central axis. At the new source skin distance of 65 cm., this point should be plotted at a depth of 10.5 cm.

B. *All Other Shapes.* (*a*) *At the normalized source skin distance.* For a rectangular field of axes size 7×10 cm. at the normalized source skin distance of 55 cm. proceed as follows: (1) Plot the central axis depth dose curve for an area given by the square of the axis in the plane of which the isodose distribution is required. That is, plot the central axis depth dose curve for an area of 49 sq. cm. at a source skin distance of 55 cm. (2) On the same graph plot the central axis depth dose curve for the actual area to be used, in this case 70 sq. cm. (3) From this graph read off the change in depth of any given percentage depth dose value; once again these corrections are applied to the data of Figures 1 to 5. The change in depth from the square field of 7×7 cm. to the rectangular field of 7×10 cm. is an increase of 3 mm. at a depth of 10 cm. From Figure 3 it is found again that the position of the 10 per cent contour for a 7 cm. axis size is 4.8 cm. from the central axis. This contour for the rectangular field is therefore plotted at a depth of 10.3 cm. (*b*) *At other than the normalized source skin distance.* Let us take as an example the determination of the distribution for a 7×10 cm. field at a source skin distance of 65 cm. (refer to Fig. 8 and 9). (1) and (2) Proceed as for B (a) (1) and (2) above. (3) From Figure 7 determine the depth corrections for a source skin distance of 65 cm. and apply these corrections to the depth dose curve for a 7×10 cm. field at 55 cm. source skin distance. The changes in depth between the curve for 7×7 cm. at 55 cm. source skin and that for 7×10 cm. at 55 cm. source skin distance are then read off. These corrections are then applied to the data in Figures 1 to 5 as previously.

C. *Elongated Fields.* As pointed out by Jones[3] and by Wilson and Perry,[9] the central axis depth dose distribution for an elongated area differs from that of the

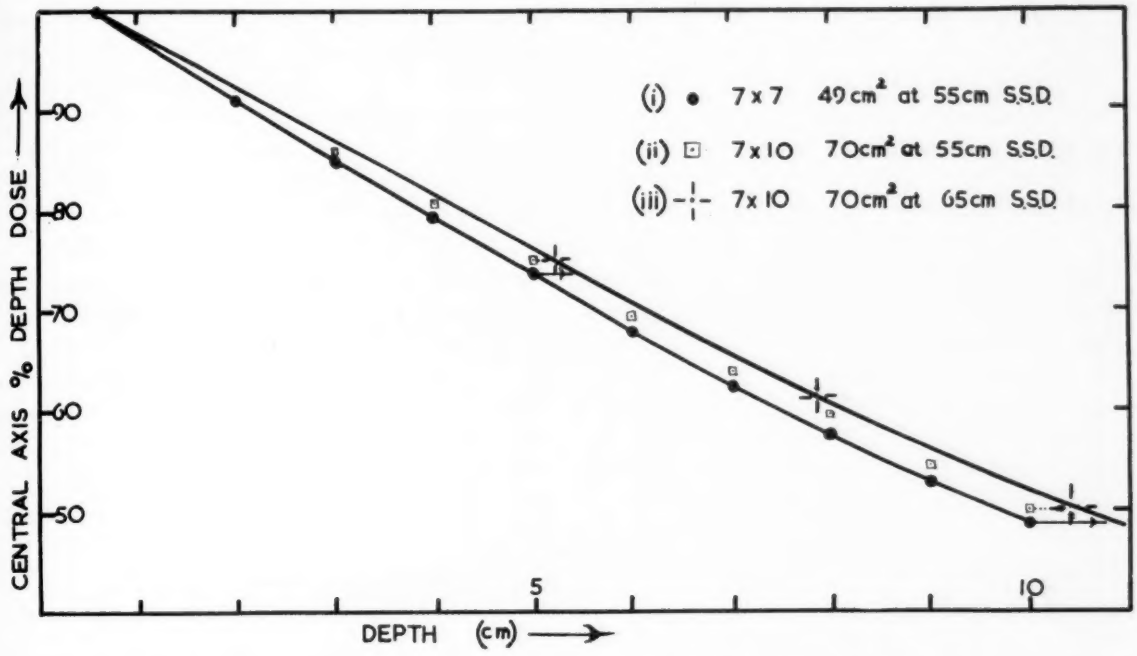

Fig. 8. Determination of the distribution for a 7×7 cm. and a 7×10 cm. Co^{60} field at 55 cm. source skin distance and a 7×10 cm. field at 65 cm. source skin distance.

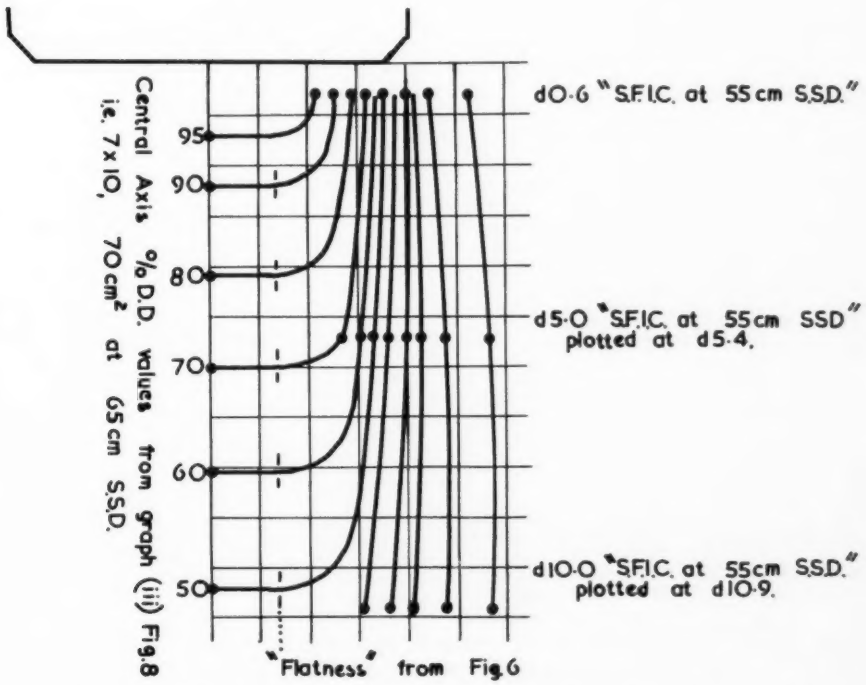

Fig. 9. Determination of the distribution for a 7×10 cm. Co^{60} field at 65 cm. source skin distance (central axis percentage depth dose values from Graph III of Figure 8 and beam flatness from Figure 6).

equivalent area owing to the change in the scatter pattern. In these circumstances there is defined an "effective area," which is the circular area giving the same central backscatter as the field in question. Data for obtaining this area are given by Jones[3] and by Wilson and Perry[9] for various energy ranges. In determining the distributions for an elongated field of this type the procedure above is used, the central axis depth dose curve required being that for the appropriate effective area.

The foregoing information was obtained with the cobalt 60 unit, the source in which was of 1.5 cm. diameter. It was found that the distributions outside the geometric edge of the beam could be determined from the data of Figures 1 to 5. In other circumstances where the focal spot size is small and collimation good, a discontinuity will be evident at the geometric edge. To determine the distributions in the scatter region in such circumstances, other information is necessary.

An examination of the scatter outside the geometric edge was carried out using the Meredith and Neary[7] analysis. It was found that the ratio of scatter for a rectangular field (Y cm. × X cm.) to that for a square field (Y^2) plotted against the ratio of the field axis was constant, independent of the depth of the observation or the quality between half-value layers of 1 mm. of copper and 3.6 mm. of copper. This analysis was confirmed by the experimental observations of Martin and Evans.[5] In use for determining the scatter distribution outside the 7 cm. edge of a 7×10 cm. field, for example, the appropriate correction factor for the axes ratio (Y/X) is determined from the curve of Figure 10. The scatter level for the square field measuring

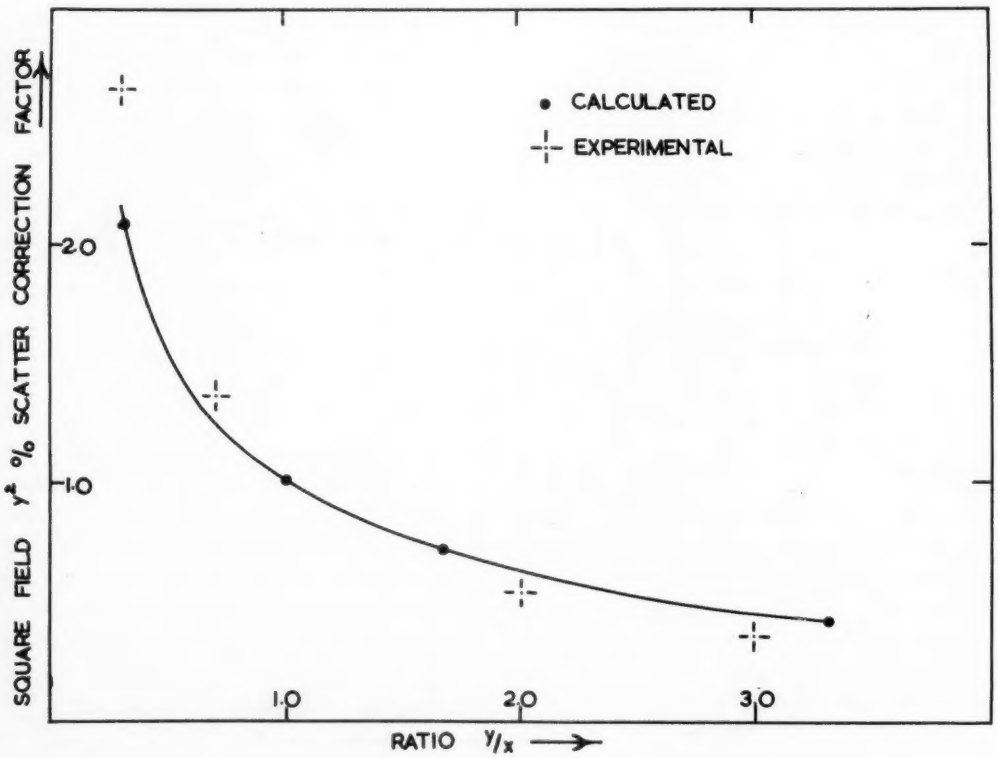

FIG. 10. Scatter correction factor for discontinuous type of isodoses between 1.0 mm. Cu half value layer and 3.6 mm. Cu half value layer.

$$\left[\frac{\text{square field } (Y^2)\% \text{ scatter}}{\text{elongated field } (Y\times X)\% \text{ scatter}} \text{ against elongation ratio } \left(\frac{Y}{X}\right)\right].$$

7×7 cm. is then multiplied by this factor to give the new value of the scatter contribution at this position.

SUMMARY

Normally, producing isodose distributions for a wide range of field sizes and other beam factors requires extensive measurement or calculation.

A simple method of obtaining isodose distributions is described. It is dependent on graphical data derived from a minimum of experimental or published information, which should include isodose distributions for three square or circular fields at the appropriate source skin distance and beam quality in use, together with a collection of central axis depth dose data. No further calculation is required.

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I am indebted to Dr. J. H. Martin for his help and interest in the development of the method; to Mr. K. L. Biggs, and the staff of the Peter MacCallum Clinic, Launceston, Tasmania, with whom I worked to obtain the necessary data; and to Miss B. Rose and Miss G. Muller for their assistance with the calculations.

REFERENCES

1. Central axis depth dose data. *Brit. J. Radiol.*, 1953, Suppl. 5.
2. Diagrams and data scheme. Hospital Physicists' Association. Great Britain.
3. Jones, D. E. A. Note on back-scatter and depth doses for elongated rectangular x-ray fields. *Brit. J. Radiol.*, 1949, *22*, 342–345.
4. Martin, J. H. Computer for x-ray isodose curve production. *Brit. J. Radiol.*, 1946, *19*, 343–346.
5. Martin, J. H., and Evans, E. A. Radiation outside defined field. *Brit. J. Radiol.* To be published.
6. Mayneord, W. V., and Lamerton, L. F. Survey of depth dose data. *Brit. J. Radiol.*, 1941, *14*, 255–264.
7. Meredith, W. J., and Neary, G. J. Production of isodose curves and calculation of energy absorption from standard depth dose data. Part I and Part II. *Brit. J. Radiol.*, 1944, *17*, 75–82 and 126–130
8. Wheatley, B. M. Instrument for dosage estimation with fields of any size and shape. *Brit. J. Radiol.*, 1951, *24*, 388–391.
9. Wilson, C. W., and Perry, B. J. Physical observations relating to 2 MeV Van de Graaff electrostatic generator at Westminster Hospital. *Brit. J. Radiol.*, 1952, *25*, 210–219.
10. Worthley, B. W., Tooze, J., Brown, J., and Fry, R. Dosage estimation in radiotherapy. *Acta radiol.*, 1955, Suppl. 128.

SOME CLINICALLY USEFUL DATA FOR FIXED FIELD AND ROTATIONAL TELECOBALT THERAPY*

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THE purpose of this paper is to present clinically useful data for the application of cobalt 60 beam therapy. All of the data were experimentally determined with a Keleket-Barnes rotating unit, equipped with a variable collimator and a cobalt 60 source 2 cm. in diameter. As will be described below, these data are applicable to other equipment having similar dimensions and collimating system.

The distance from the source to the axis of rotation is 60 cm. The front face of the variable collimator is 30 cm. from the source. The four shutter blocks of the collimator are 8.5 cm. thick and are designed so as to travel on the surface of a sphere rather than on a plane as in the case with the more familiar del Regato localizer. This type of motion permits the edge of the shutter blocks always to remain parallel to the geometric edge of the beam and thus serves to reduce the amount of penumbra.

The light localizer consists of an arrangement of two mirrors, one serving as a light source and the other as a reflector to make the optical path to the diaphragm equivalent to that of the cobalt 60 source. The collimator system is schematically illustrated in Figure 1.

Because of the relatively large size of the cobalt 60 source as compared to the focal spot of a roentgen-ray tube and also because of variations in the amount of radiation scattered from the collimating system, the air dose rate will vary with the field size. This variation is not remarkable for field sizes greater than 50 cm.^{2} but must be taken into account for fields smaller than this.

For the same reasons stated above, the air dose rate for this unit decreases approximately, but not exactly, according to the inverse square law. Measurements have demonstrated that when the inverse square law is used to calculate the output at 80 cm. source-detector distance, the result will be 4 per cent greater than would be measured. Table 1 gives data relating the output for various field sizes to the output at different source-detector distances. The 100 cm.^{2} field, at 60 cm. source-skin distance is taken as a reference point.

TABLE I

PER CENT VARIATION OF OUTPUT RELATIVE TO FIELD SIZE

Source-Detector Distance	Field Size in Sq. Cm.					
	10	25	50	100	225	400
50 cm.	123	138	142	148	152	154
60 cm.	83	93.5	96	100	103	104
80 cm.	45	50.5	52	54	56	57

Figure 2 illustrates the variation of backscatter with field size. Measurements were made with a pressdwood phantom and a 25 r Victoreen chamber with a 3 mm. plastic cap to ensure electron equilibrium. The curve compares the readings of the chamber with and without a backscattering medium for different field sizes. Although these data were obtained at 60 cm. source-skin distance, they are applicable over a wide range of source-skin distances.

The penumbra is determined by the construction of the collimator and the distance of the collimator from the skin. As the distance from the collimator to the skin is increased, the amount of penumbra also increases. It is, however, constant for a fixed set of treatment conditions and is independent of field size. Figure 3 shows the experimental curves obtained by moving a

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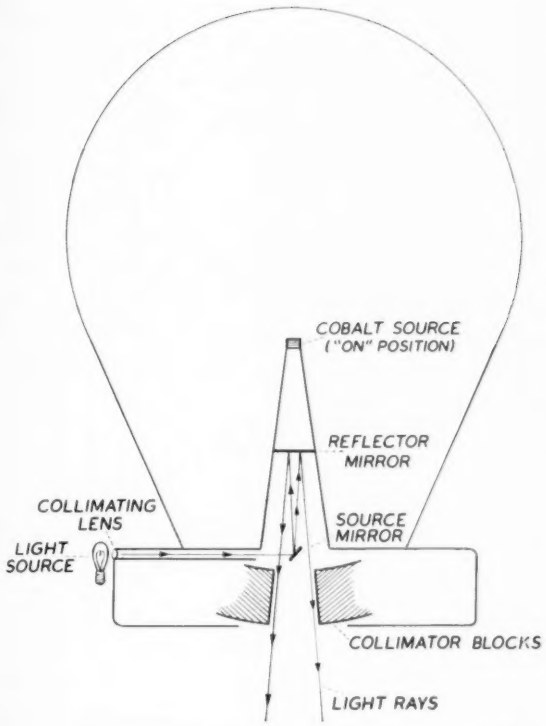

Fig. 1. Schematic diagram of cobalt 60 head illustrating collimator and light beam localizer.

detector across the beam and plotting the intensity as a function of position.

It was found that the edge of the light beam did not always correspond to the same percentage of maximum intensity. As the field size is made larger, the intensity at the edge of the light beam also becomes larger. The reason for this was found to be due to a difference in the optical and gamma ray path lengths where the optical path was found to be 34 cm. and the distance of the cobalt 60 source to the front face of the collimator 30 cm.

Although the light localizer indicates that the treatment field has sharp corners, measurements show that the corners of the treatment beam are actually rounded. This usually introduces no treatment problems since only the extreme corners are affected. Figure 4 shows the dose distribution in a plane perpendicular to the beam axis located at a depth of 5 mm. beneath the surface for four different field sizes.

Using a pressdwood phantom and an automatic field mapping device,[4] a series of isodose curves were made at 60 cm. source-skin distance. These are illustrated in Figures 5 through 13. Figures 12 and 13 represent split fields made with different thicknesses of lead strips having the same width. They can be used, for example, in the case of external treatment of the pelvis following radium application.

Tumor dose calculations for rotation therapy are performed utilizing the technique previously described by Braestrup and Mooney[1] and Johns and co-workers.[2,3]

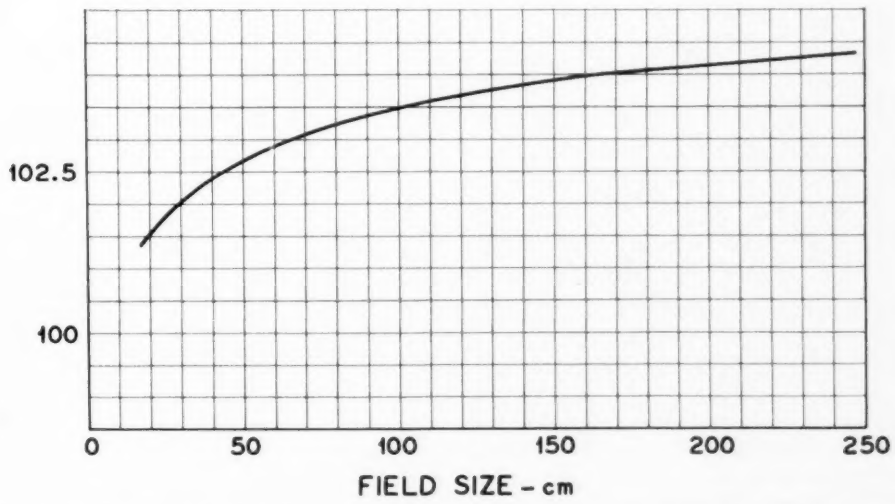

Fig. 2. Variation of backscatter with field size. Field size defined by light beam localizer. Surface dose as per cent of air dose. Source-skin distance 60 cm.

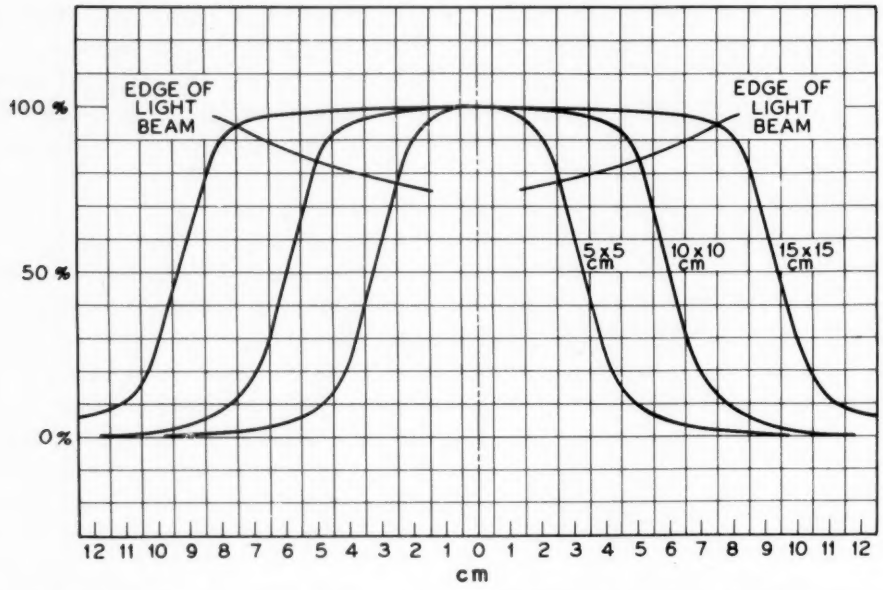

FIG. 3. Plots of intensity versus distance from axis of beam for three field sizes. Scans made at a depth of 0.5 cm. in a 15 cm. masonite phantom. Source-skin distance 60 cm.

Absorption curves for obtaining the tumor-air ratio have been experimentally determined and are illustrated in Figure 14. When calculating the central axis dose, it was found that the final figure must be reduced by 4 per cent because of absorption by the treatment table.

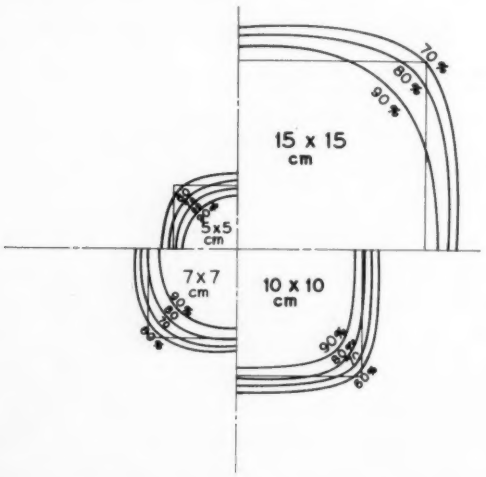

FIG. 4. Dose distribution in a plane 0.5 mm. below the surface for four field sizes. Axis of the incident beam perpendicular to the plane of the paper. Edge of light beam indicated by straight solid lines. Only one quarter of entire field shown. Source-skin distance 60 cm.

It is often necessary to know the dose delivered to points not on the axis of rotation. Mainly because off-axis points are

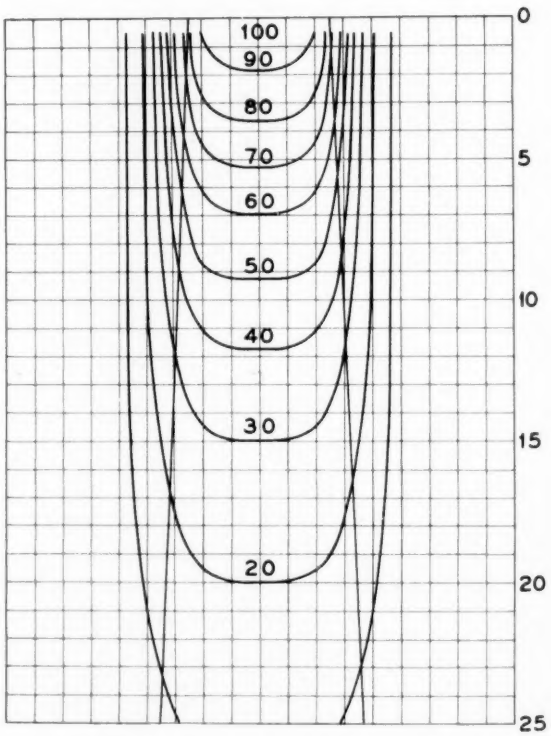

FIG. 5. Isodose curves for 5×5 cm. field size. Source-skin distance 60 cm.

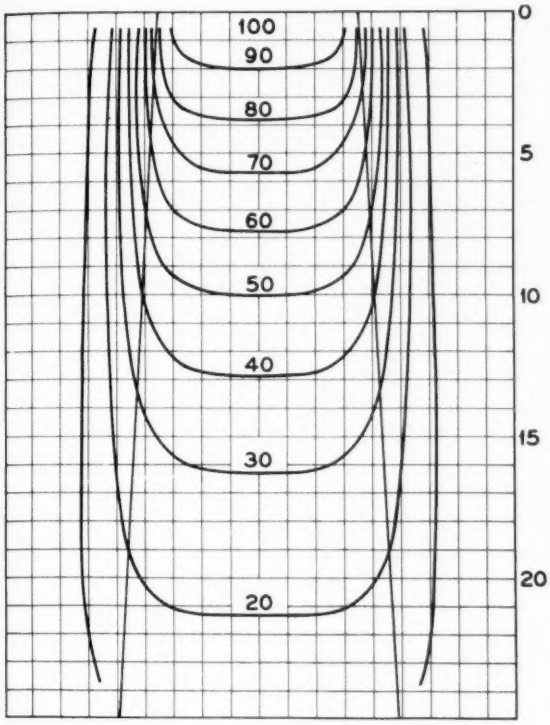

Fig. 6. Isodose curves for 7×7 cm. field size. Source-skin distance 60 cm.

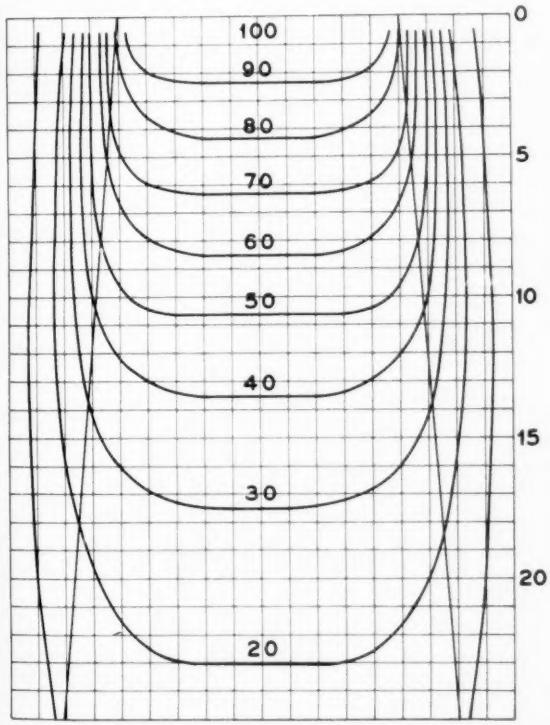

Fig. 7. Isodose curves for 10×10 cm. field size. Source-skin distance 60 cm.

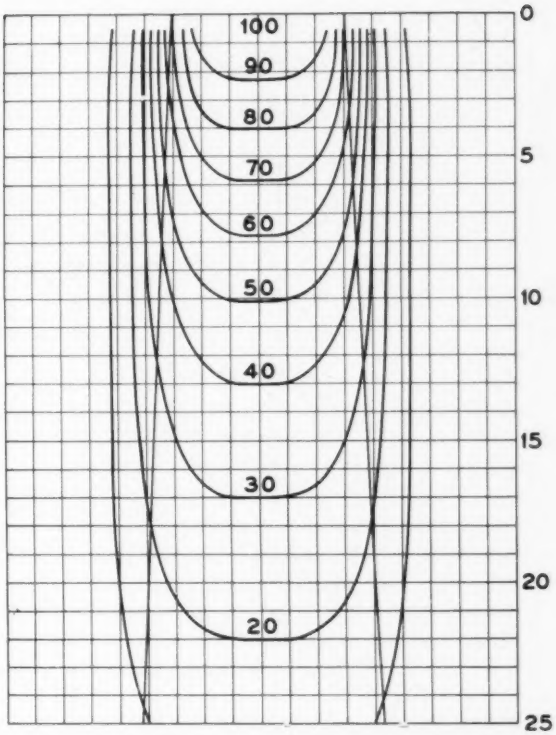

Fig. 8. Isodose curves for 6×15 cm. field size. Source-skin distance 60 cm.

sometimes in and sometimes out of the beam, the calculation of dose to these points is a good deal more complicated than calculation of dose to the axis of rotation. The following procedure has been devised in order to reduce the mathematical complexities of the problem. Although several simplifying assumptions have been made, measurements indicate that they do not introduce great error.

After locating the point under consideration on the same cross section used for the calculation of tumor dose, the distance (d) from the axis of rotation to the point must be measured. From Figure 3 the 50 per cent width (b) of the treatment beam at 60 cm. source-skin distance can be determined. The 50 per cent width is the diameter of the beam when the intensity has dropped to one half of the maximum intensity, *e.g.*, the 50 per cent width of a 10×10 cm. field is 12 cm. The ratio of "b" over "d" determines the fraction of one complete turn during which the off-axis point will be in the radi-

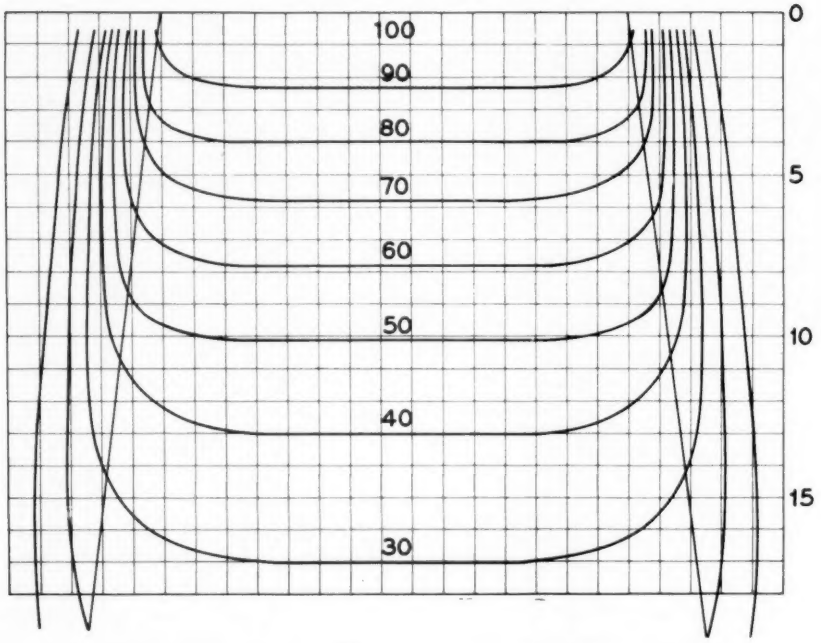

FIG. 9. Isodose curves for $6\times\overline{15}$ cm. field size. Source-skin distance 60 cm.

ation beam when either closer to or farther from the source than the axis of rotation. Table II shows a variety of ratios and their corresponding angles.

The dose rate at the point is also dependent on the distance of the point from the source and will vary according to the inverse square law. Because the output will be known at the axis of rotation, it is convenient to take it as a reference point. The inverse square law factors for conditions when the point is closer to or farther from the

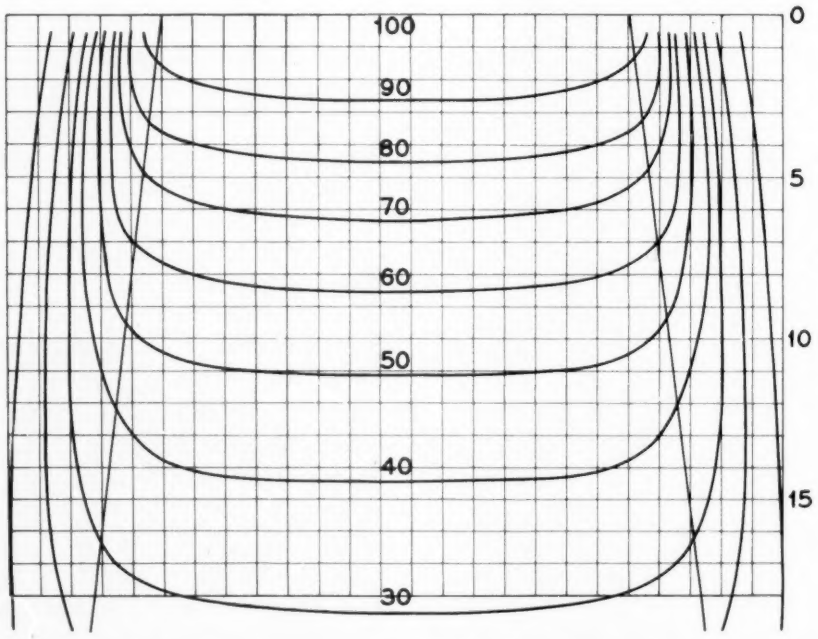

FIG. 10. Isodose curves for 15×15 cm. field size. Source-skin distance 60 cm.

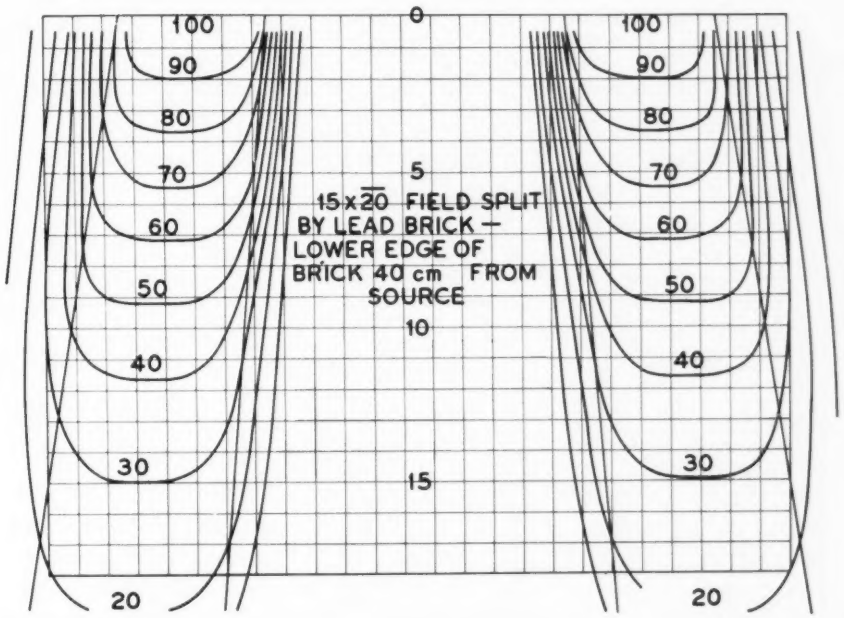

FIG. 11. Isodose curves for $15 \times \overline{20}$ cm. field split by lead block 5 cm. wide. Source-skin distance 60 cm.

source than the axis are listed in Table III.

Lastly, the tissue absorption factors must be determined. Since the amount of intervening tissue between the point and the source will vary considerably as the source rotates, average absorption factors must be used. These may be determined with the aid of the tumor-air ratio curves shown in Figure 5. Unless there are large variations in tissue thickness when the point is in the direct beam, an average of three measurements gives sufficient accuracy.

The equations for calculation of off-axis dose are given at the top of the next page.

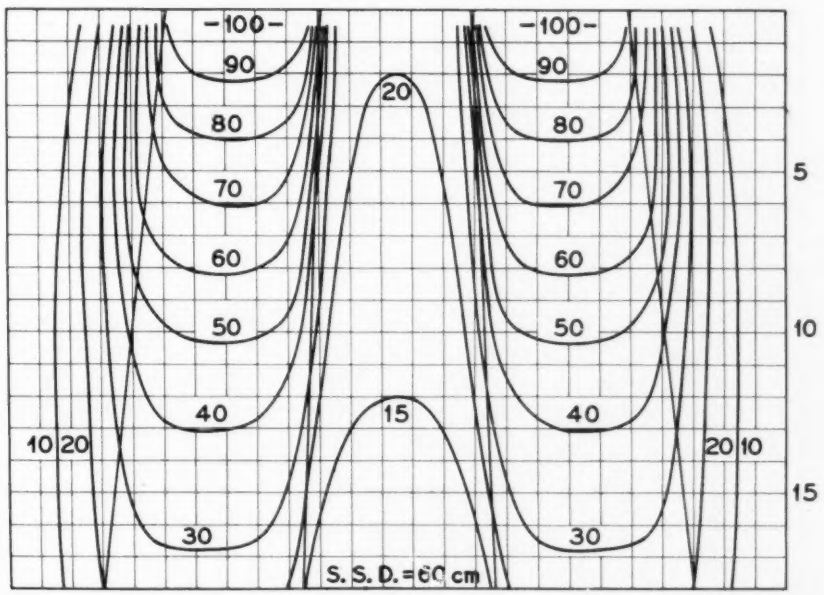

FIG. 12. Isodose curves for 15×15 cm. field split by lead block 3.3 cm. wide and 2.4 cm. thick. Lower edge of lead 40 cm. from source. Source-skin distance 60 cm.

Point closer to source than axis

$$\frac{\text{Angle}}{360^\circ} \times (\text{Inverse square factor})\text{-closer} \times (\text{Tissue absorption factor})\text{-closer}$$

$$\times (\text{r/min. at axis}) \times (\text{treatment time}) = \text{dose to point.}$$

Point farther from source than axis

$$\frac{\text{Angle}}{360^\circ} \times (\text{Inverse square factor})\text{-farther} \times (\text{Tissue absorption factor})\text{-farther}$$

$$\times (\text{r/min. at axis}) \times (\text{treatment time}) = \text{dose to point.}$$

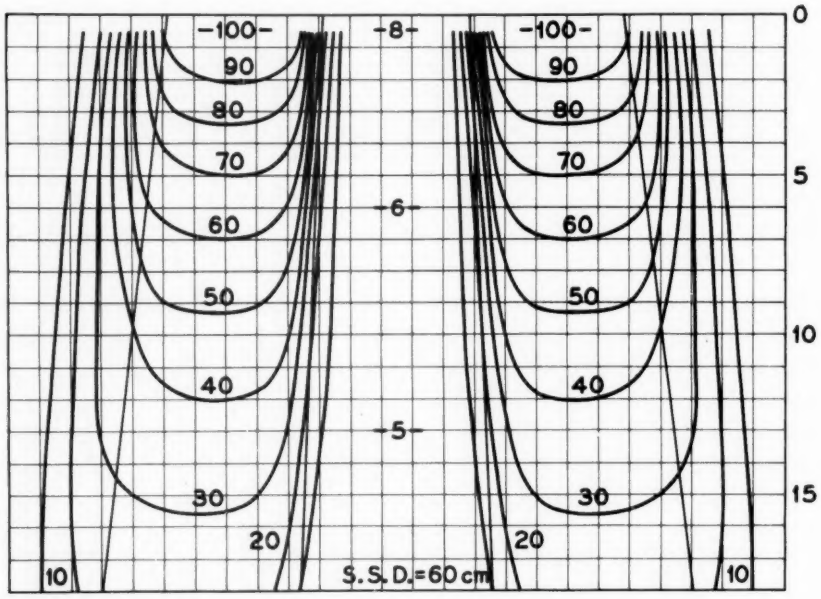

FIG. 13. Isodose curves for 15×15 cm. field split by lead block 3.3 cm. wide and 4 cm. thick. Lower edge of lead 40 cm. from source. Source-skin distance 60 cm.

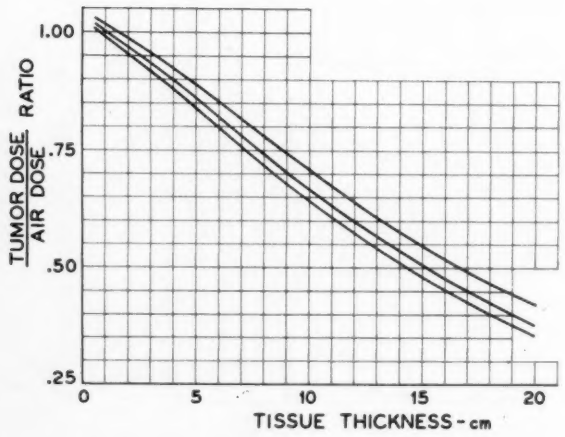

FIG. 14. Curves illustrating the tumor-air dose ratio versus tissue thickness for three field sizes with rotation therapy. The curves include the back-scatter in the air dose reading. Source-detector distance 60 cm. *Upper curve:* 10×10 cm. field. *Middle curve:* 7×7 cm. field. *Lower curve:* 5×5 cm. field.

Table II

b/d	Angle	b/d	Angle
.4	23°	1.3	81°
.5	29°	1.4	89°
.6	35°	1.5	97°
.7	41°	1.6	106°
.8	47°	1.7	116°
.9	53°	1.8	128°
1.0	60°	1.9	144°
1.1	67°	2.0	180°
1.2	74°		

The results of the two equations must be added to obtain the total dose. The equations are valid only if an integral number of rotations are made per treatment.

In order to use the above data for units with construction comparable to that of the Keleket rotary, the following factors must be taken into account: (1) Differences in collimator construction and source diameter; (2) position of the edge of the light beam in relation to the edge of the gamma-ray beam; (3) radius of rotation of the source.

Since the extent of penumbra depends directly upon the source size and source-collimator distance, straight geometric corrections may be used to adjust the above data to units with different physical parameters.

It is the author's (R.J.S.) experience that there is considerable variation in the relative positions of the edges of the light and gamma-ray beams among units of different manufactures. These variations will result in different effective field sizes, the differences being more pronounced for the smaller fields. In order to use the above isodose curves correctly, one must first locate the position of the gamma-ray beam in relation to the light beam on his unit.

Table III

Distance (d) from Axis of Rotation	Inverse Square Law Factors		(60 Cm. Source-Axis Distance)
	Closer	Farther	
(cm.)			
3	1.11	.91	
4	1.15	.88	
5	1.19	.86	
6	1.24	.83	
7	1.28	.80	
8	1.33	.78	
9	1.39	.76	
10	1.44	.74	
11	1.50	.72	
12	1.56	.70	

Variations of the radius of rotation need be taken into account only when determinations are made for off-axis points. If these variations are not greater than ± 5 cm., no serious errors will be introduced by using the data presented.

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REFERENCES

1. Braestrup, C. B., and Mooney, R. T. Physical aspects of rotating telecobalt equipment. *Radiology*, 1955, *64*, 17–27.
2. Johns, H. E. Physical aspects of rotation therapy. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1958, *79*, 373–381.
3. Johns, H. E., Morrison, M. T., and Whitmore, G. F. Dosage calculations for rotation therapy; with special reference to cobalt 60. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1956, *75*, 1105–1116.
4. Schulz, R. J. Automatic field mapping device. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1956, *76*, 939–941.

THE ADVANTAGES AND LIMITATIONS OF COBALT 60 HECTOCURIE TELETHERAPY*

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THE advantages and limitations of cobalt 60 teletherapy in general are now fairly well understood by the radiologist. Occasional bursts of enthusiasm by the lay press distort and exaggerate the benefits derived from this form of irradiation, but the radiotherapist realizes that the true value lies somewhere between the exaggeration of the lay press and the iconoclasm of the over-conservative radiologist.[2]

ADVANTAGES

The advantages which may result from the use of cobalt 60 teletherapy are predictable by the radiotherapist because of his knowledge of the physics of cobalt 60 radiation and because of the decades of his experience with supervoltage roentgen-ray machines and radium teletherapy units. The radiotherapist would indeed find it strange if cobalt 60 teletherapy should result in many more "cures" of cancer than other radiation methods have yielded.[3] The beneficial features of cobalt 60 teletherapy are familiar even to those radiotherapists who have not yet had the chance to use it. These include: (1) skin sparing; (2) increased depth dose; (3) lessened bone absorption; (4) decreased side scatter; and (5) simplicity of operation.

Skin sparing of the cobalt 60 beam is by far its most advantageous characteristic. It allows high dosage through single portals, and sometimes this skin sparing provides access with radiation to lesions which are not usually considered treatable. For example, the rather common carcinoma of the rectum, either the postoperative recurrence or the locally unresectable lesion in the hollow of the sacrum is exceedingly difficult to treat unless the skin over the sacrum can be spared. Increased survival in such instances may be too much to expect, but palliation of pain and control of bleeding are far more often achieved with cobalt 60 teletherapy than with irradiation in the "conventional" range. The skin has never been a real deterrent to the treatment of "curable" cancer with 200 kv. radiation, for skin damage is a small price to pay for survival. But skin damage is indeed a high price to pay for attempt to palliate. With 200 kv. roentgen therapy, dosage to a rectal carcinoma is often limited by the inability of the patient with a colostomy to tolerate a discomforting skin reaction over the sacrum.

The skin sparing effect of cobalt 60 radiation allows the use of high dosage through single portals and enables simplified and efficient treatment of other relatively superficial lesions. As an example, it is difficult or impossible to treat the thyroid gland with a dose of more than 3,500 r with conventional radiation, but a single direct portal with cobalt 60 teletherapy can receive a dose of 6,000 r in the thyroid region with no appreciable effect on the skin. When single portal treatment is used, the tissue deep to the tumor may be relatively spared by shortening the source skin distance. However, if the source skin distance is short, the dose to the surface of the skin is relatively increased by the secondary electrons from the walls of the cone or collimator, and these should be filtered by a thin brass filter placed at the cone end.

The increase in depth dose with cobalt 60 teletherapy is too often considered to be the major advantage of this form of therapy, although there are no deep seated lesions which cannot receive a cancerocidal dose with 200 kv. radiation with multiple fields or rotation. We are limited in dosage of deep seated lesions by the radiosensitivity of adjacent organs, not by the lack of

* Presented at the Fifty-eighth Annual Meeting of the American Roentgen Ray Society, Washington, D. C., October 1–4, 1957.

penetrability of our rays. As examples of this, carcinoma of the ovary in the pelvis can be given only a dose which the intestine can tolerate. The tolerance of these normal tissues is not greater for cobalt 60 than for conventional radiation. It has been shown that depth doses for cobalt 60 are greater than for 200 kv. roentgen rays, and, at times, this has been unfairly stressed by comparing depth doses at different distances. At a source skin distance of 30 cm. the depth doses of cobalt 60 are not unlike those of 200 kv. (1.0 mm. Cu half-value layer) at 50 cm. target skin distance, and at a distance of 50 cm. not unlike 200 kv. at 80 cm. There is no reason to change from 200 kv. to cobalt 60 therapy for depth dose increase alone when this could be achieved more simply by increasing the target skin distance with 200 kv. roentgen rays.

Another advantage of cobalt 60 teletherapy is the lessened absorption of radiation by bone. This phenomenon increases the dose to tissues beneath bone, such as brain and pelvic organs. It has also been felt that radionecrosis of bone may be lessened. Radionecrosis of the jaw has, however, been observed after cobalt 60 and other forms of supervoltage irradiation and may even increase in incidence because of our tendency to give larger doses when using supervoltage irradiation.

The decreased side scatter of the cobalt 60 beam is presumed to account for lessened radiation sickness. Our own experience in the treatment of 600 patients with a cobalt 60 hectocurie unit in the past three years bears out this presumption. Radiation sickness is most difficult to evaluate clinically, but we find ourselves giving larger doses at each treatment and giving fewer patients medication for nausea or vomiting. Some of this improvement may be attributed to our tendency to use smaller fields with cobalt 60 than with 200 kv. roentgen therapy.

A cobalt 60 hectocurie apparatus is far simpler to operate than 200 kv. or supervoltage roentgen-ray machines. This advantage is particularly striking when the two forms of treatment are employed concurrently. It has been stated that cobalt 60 teletherapy should not be used without the services of a physicist, but it is our impression that the physicist is just as necessary with 200 kv. apparatus. To the nonphysicists the electronic circuitry of the 200 kv. machine and the spectral distribution of the roentgen rays produced by it are puzzling, while the lead enclosure housing the radioactive cobalt source is more easily understood. The anxiety over the accuracy of output of roentgen-ray machines and the frequent need for recalibration are absent with cobalt 60 teletherapy units. Only in the planning of protection of an installation is the physicists's task more exacting with cobalt 60 than with 200 kv. roentgen-ray installations.

Of all the advantages of cobalt 60 teletherapy, skin sparing is most important, and it gives the radiotherapist an opportunity to treat to higher dose levels through a single field. As an example, a patient with carcinoma of the middle ear (Fig. 1, *a* and *b*) was treated directly through the pinna with a single portal to a tumor dose of 6,000 r in six weeks with cobalt 60 teletherapy. The minor skin effect is an advantage of cobalt 60 radiation, but even more important is the question of how else such a patient could have been treated. Squamous cell carcinoma of the middle ear has not previously responded in our experience to attempts to treat with intra-aural radium or multiple field roentgen therapy. The simplest way seems to be with a single portal of penetrating skin sparing radiation. A similar principle is involved in the treatment of lesions of the lymph nodes of the neck, axilla or groin and of the parotid and thyroid glands.

LIMITATIONS

Among the limitations of cobalt 60 hectocurie therapy, as compared to 200 kv. roentgen therapy, may been umerated: (1) unsuitability for intraoral (and intravaginal) therapy; (2) unsuitability for treatment of skin cancer; (3) reduced use-

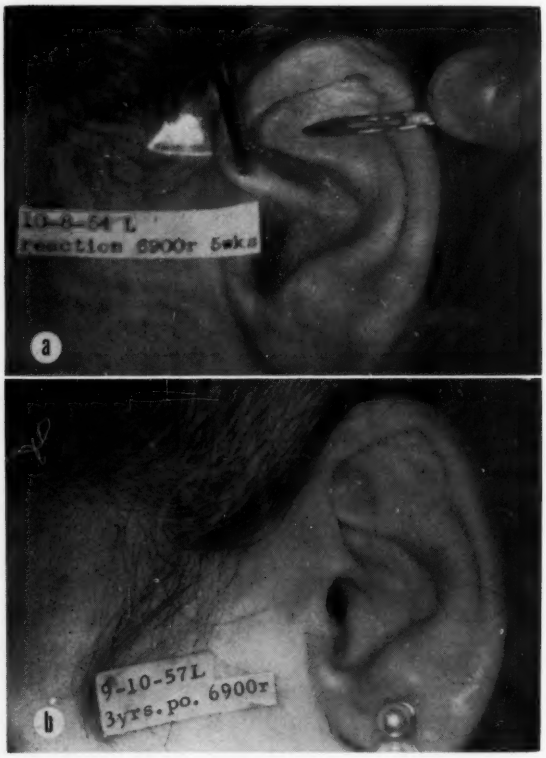

FIG. 1. (*a*) Appearance of the skin of a patient with carcinoma of the middle ear at the height of reaction on the day of completion of cobalt 60 irradiation. An exposure dose of 6,900 r (in air at the skin) had been delivered in five weeks through a single circular portal 5 cm. in diameter, and the source skin distance was 35 cm. The estimated tumor dose was 6,000 r. Moist desquamation of the skin was present between the separated crura as indicated in this illustration. Similar moist desquamation was present within the external auditory canal. Even at the height of reaction the skin surface has little reaction. (*b*) Three years after treatment the external ear shows no evidence of sequelae of the previous therapy.

fulness of the large fields; (4) too much penumbra at long source skin distances; and (5) requirement of radiation protection of operating personnel.

Certain intraoral carcinomas of the tongue, buccal mucosa or gingiva are successfully treated by intraoral roentgen-ray cones, which cannot be done with present cobalt 60 teletherapy apparatus. The use of cobalt 60 teletherapy in such small lesions would involve useless irradiation of too much normal tissue. Other intraoral lesions are more adequately treated with implantation of radium.

By the very nature of the skin sparing effect, cobalt 60 teletherapy is unsuitable for the treatment of superficial skin cancer. Maximum dose level and electron equilibrium are reached at a depth of about 5 mm. of tissue, too deep for many skin cancers. These lesions are, in general, much better treated with 45 to 100 kv. roentgen rays at short target skin distances.

The size of useful fields at comparable distances is smaller with cobalt 60 hectocurie units than with 200 kv. roentgen therapy. Few cobalt 60 machines yield fields as large as 20 by 20 cm. at 50 cm. source skin distance. At these distances the geometric penumbra is large, and with large portals the splay of the beam is pronounced. Overlapping adjacent portals due to crossing of the transmarginal radiation at depth must be avoided in treatment plans, because of the tendency to go to higher dose levels with the cobalt 60 radiation. Such problems are encountered in the treatment of the abdomen for seminoma of the testicle or carcinoma of the ovary.

Protection remains the most serious problem in cobalt 60 teletherapy. As the permissible dose levels of radiation are continuously being lowered, one would feel more secure if the irradiation could be interrupted by the simple break of an electric current. This is not so with the cobalt 60 units, for even in the "off" position, emission of minimal radiation continues. The acid test is in the actual measurement of radiation received by the personnel using the machine. In our experience physicians and technicians operating a hectocurie unit receive average exposures of less than 50 mr per month on their film badges and pocket dosimeters. It is gratifying to observe that radiation personnel in daily contact with a 500 curie cobalt 60 unit in the treatment of patients has received less than 500 mr per year in the past three years (Table 1).

TABLE I

EXPOSURE TO RADIATION OF PERSONNEL FROM A HECTOCURIE COBALT 60 UNIT

	Film Badge Readings		Pocket Dosimeter Readings	
	mr/yr.	Average mr/wk.	mr/yr.	Average mr/wk.
Dr. A	650	13		
Dr. B	500	10	480	10
Dr. C	360	7		
Cobalt Technician	480	10	480	10
Maximum Permissible	5,000	100		

Listed personnel were exposed to a hectocurie cobalt 60 apparatus daily. The exposures were determined by monthly reading of film badges from January, 1956 to July, 1957. Some of the exposure on the doctors' film badges was received by radiation other than cobalt 60. The radiation received by the personnel has been about one-tenth of the maximum permissible dose.

DISCUSSION

Observations previously made with million volt roentgen therapy have indicated that subcutaneous fibrosis may be a serious problem with supervoltage irradiation.[1] Late board-like rigidity and even sarcomas of the abdominal wall have been reported. Our own experience is short (only three years), but we have treated many patients with exposure doses of 6,000 r and more to a single field in six weeks or less. As yet we have seen no subcutaneous fibrosis detectable by palpation except in those few instances where skin reactions were deliberately induced. In an attempt to determine the need for an electron filter[2] at the end of the treatment cone, single portals were treated with an open cone applied directly to the skin. Part of the skin was covered

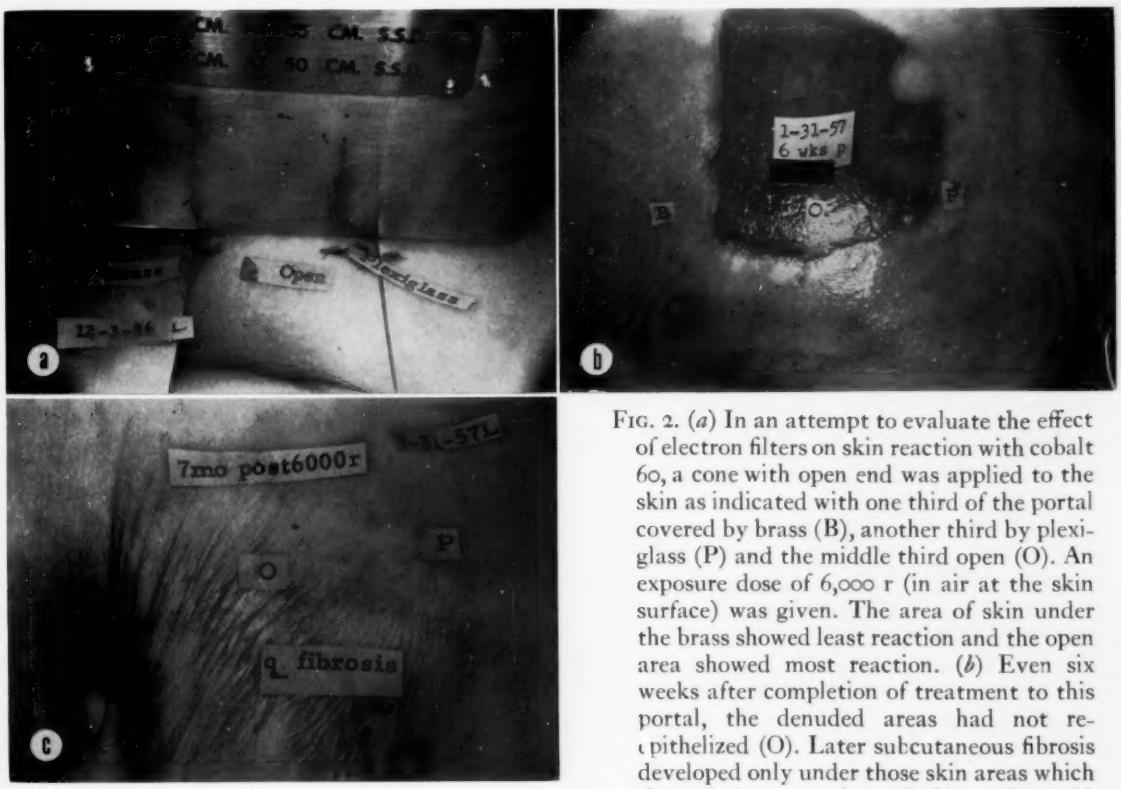

FIG. 2. (*a*) In an attempt to evaluate the effect of electron filters on skin reaction with cobalt 60, a cone with open end was applied to the skin as indicated with one third of the portal covered by brass (B), another third by plexiglass (P) and the middle third open (O). An exposure dose of 6,000 r (in air at the skin surface) was given. The area of skin under the brass showed least reaction and the open area showed most reaction. (*b*) Even six weeks after completion of treatment to this portal, the denuded areas had not re-epithelized (O). Later subcutaneous fibrosis developed only under those skin areas which showed desquamation of the surface. (*c*) This experiment showed the efficiency of brass as an electron filter and also indicated an association between subcutaneous fibrosis (q) and overlying severe skin reaction.

with plexiglass and another part with brass. The middle of the field remained open. When an exposure dose of 6,000 r was given in four weeks, the skin reaction was severe where uncovered, much milder under the plexiglass, and barely discernible under the brass (Fig. 2, *a*, *b* and *c*). After several months the skin under the "open" area re-epithelized, and subsequently there developed a marked subcutaneous fibrosis under this skin area, but *not* under the skin which had been covered by the electron filters (plexiglass or brass). Although other factors may be operative, there is an association between severe skin reactions and underlying fibrosis.

The above described experiments with electron filters were carried out to help in the design of cones, particularly for treatments at short source skin distances with the hectocurie units. There are two advantages to the use of short source skin distances: (1) increased output and (2) rapid dose fall-off. These advantages can be obtained while still retaining the skin sparing feature of cobalt 60 teletherapy by closing the end of the cone with a thin sheet of brass.

An important lesion deserving special comment in relation to cobalt 60 hectocurie teletherapy is carcinoma of the larynx. Early results in 30 patients indicate as favorable a response as the best obtained with 200 kv. roentgen rays. In addition, there are certain other advantages of irradiation with cobalt 60. The patient has no skin discomfort and after a few months the epilation is the only identifying characteristic of the skin treated. If laryngectomy is indicated for persistence or recurrence of the lesion after cobalt 60 treatment, healing of the operative wound will not be seriously hampered. The relatively low morbidity, the retention of voice, and the comparatively satisfactory "cure" rate render cobalt 60 hectocurie teletherapy the treatment of choice in lesions confined to the larynx.

SUMMARY

Cobalt 60 hectocurie teletherapy has definite advantages and certain limitations as compared to 200 kv. roentgen therapy. These are discussed in detail. The advantages of skin sparing, lessened side scatter and increased depth dose are appreciable. The hoped-for cure rates may not increase significantly, but the lessened morbidity and the greater efficiency well justify the routine use of cobalt 60 irradiation in clinical practice.

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REFERENCES

1. FRIEDMAN, M. Superior value of supervoltage irradiation in special situations: Carcinoma of mouth and carcinoma of testis. *Radiology*, 1956, *67*, 484–497.
2. RICHARDSON, J. E., KERMAN, H. D., and BRUCER, M. Skin dose from cobalt 60 teletherapy unit. *Radiology*, 1954, *63*, 25–36.
3. SILVERSTONE, S. M., and SIMON, N. Advantages of cobalt-60 in practice of radiotherapy. *J. Mt. Sinai Hosp.*, 1957, *24*, 124–136.

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SIMPLE PHYSICAL CONCEPTS IN I^{131} THYROID UPTAKE AND DIFFERENTIAL STUDIES

By MARION F. MAGALOTTI, M.D.* *and* IRVIN F. HUMMON, M.D.,†
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RADIOIODINE (I^{131}) has become widely accepted as a means of studying thyroid function. It has become available in many institutions and offices because of its simplicity and the valuable clinical information obtained by its use. Although the procedure is simple, there are certain fundamentals one must be familiar with in performing a satisfactory uptake and differential study. The complex electronic circuits need not be understood by the operator, but the elementary physical factors involved in counting the tracer and the thyroid region, and in differential studies should be known for a satisfactory evaluation.

This paper will present the essential physical features of I^{131} thyroid uptake, with the exception of the physical additions that have not significantly improved the clinical method. The physical features pertaining to differential study will also be briefly discussed.

I. PHYSICAL FEATURES OF I^{131} THYROID UPTAKE

1. Detector. A scintillation tube is preferable today to a Geiger-Müller tube because of the much greater sensitivity of the former. This greater sensitivity of the scintillation tube forces the operator to be more alert to interfering radiation from the environment that was less disturbing with the less sensitive Geiger-Müller tube. Some of the scintillation tube detectors are poorly shielded from the side, producing a high background reading from radioactive sources in the vicinity, from other patients awaiting examination, or from the same patient outside the counting area.

Diagram 1 gives the figures of the isosensitivity study of a scintillation detector. The readings at various points were converted to percentage, the reading at the opening taken as 100 per cent. Note the percentage transmission through the lateral wall of the tube, posterior to the crystal. This crystal is poorly shielded, and considerable error is encountered if the "thigh" background is taken while the patient is sitting up, and the radiation from the thyroid is inadvertently read through the side wall of the detector. A difference will be noted if the "thigh" count is repeated with the patient supine which places the thyroid at a greater distance. In Diagram 11, the same scintillation detector is shown, but a cylinder of lead, one-half inch thick, has been added. Note the marked changes in the percentage transmission from the side. This crystal is now adequately shielded from background radiation.

2. Collimator. The purpose of the collimator is to reduce the "visual field" of the crystal. In other words, the crystal should

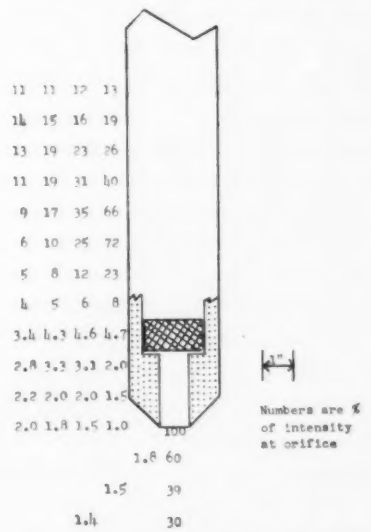

DIAGRAM I. *Isosensitivity Study.* Scintillation counter (Landauer, Magalotti).

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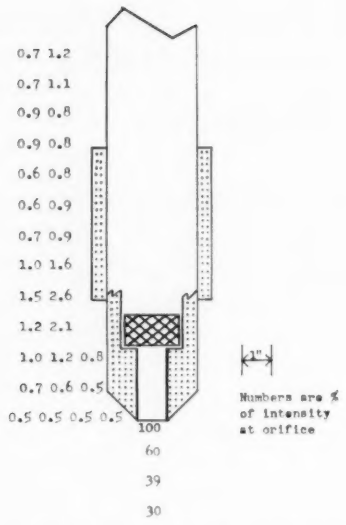

DIAGRAM II. *Isosensitivity Study*. Scintillation counter (Landauer, Magalotti).

"see" well only the area that is intended to be counted. If comparison is made with the isodose curves from a roentgen-ray tube, one may note that the isosensitivity curve from a detector is similar, being in reverse. A poorly collimated detector would read too large an area. Also, a strongly collimated detector would not be "seeing" sufficiently the desired area to be counted. Often the beginner in this field is perplexed by the fact that a collimated detector takes satisfactory counts of the tracer, but the counts from the patient's thyroid are consistently low. Therefore, it is important to check the isosensitivity of a collimated detector at the distance being used in uptake studies—a procedure which requires only a few minutes. For this purpose, a tracer is placed on a small stand, or attached to a small cardboard box with scotch tape, and positioned accurately in the central axis of the detector at a measured distance. This first reading may be taken as 100 per cent, after which readings are taken with the source moved laterally at 2 cm. stations. The counts at each point can be recorded as percentage of the central axis reading. This study will give the "fall-off" from the central axis. The opposite half of the central axis can be assumed to be the same. Diagram III shows the result of this study on two different collimators with the same scintillation tube. Note with collimator A, the readings at 4 cm. lateral to the central axis fall off to 25 per cent at 20 cm. distance and 71 per cent at 30 cm. distance. At 30 cm. distance, this value may be acceptable if the thyroid is less than 8 cm. in its frontal plane diameter and the detector is carefully aimed, whereas at 20 cm. it would be unsatisfactory. With collimator B, the readings 4 cm. lateral to the central axis fall off to 91 per cent at 20 cm. distance, but show no significant fall-off at 25 cm. and 30 cm. Thus with collimator B, a thyroid 8 cm. in its frontal plane diameter would be well covered at 25 cm. and 30 cm. and satisfactorily enough even at 20 cm. distance. If one owns the type of collimator A discussed above, it can be improved on a lathe of a machine shop by increasing the diameter and flare of the tunnel.

3. Distance. The isosensitivity study of the collimator will guide in choosing the proper distance from the detector to the thyroid. The inverse-square-law plays an important role here as to the amount of the tracer required. One can generally state that the proper distance is one that will allow the collimated detector to "see" the thyroid satisfactorily and also permit a sufficiently high count (approximately fifty times background is sufficient). The greater the distance used, the less effect the depth of the thyroid has on the reading.

4. Filter. If a discriminator is not used, soft scattered radiation reaching the crystal can be minimized by using an "A" filter of 1/16 inch lead at the aperture of the collimator. Many detectors will show no significant difference in uptakes with and without this filter. This should be determined for each installation, and the filter should be used if found advisable.

5. Recorder. Either a rate meter or scaler is satisfactory for recording, the scaler being preferable. A binary scaler has in the past been considered superior, but today the decimal scaler is used more frequently because of its dependability and ease to

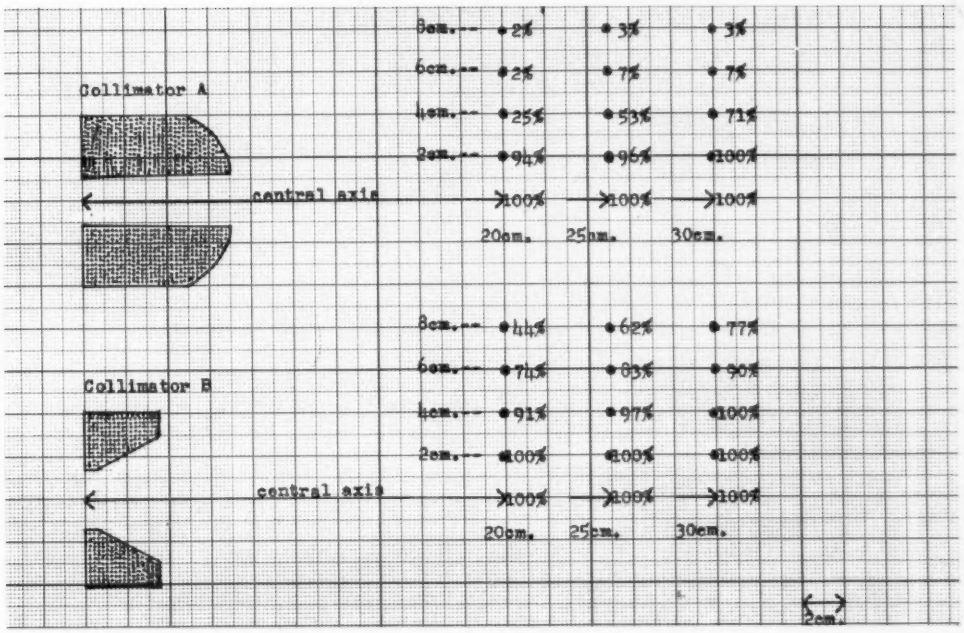

DIAGRAM III. *Isosensitivity Study.* Fall-off from the central axis at various distances from detector with two different collimators.

read. Practically all new recorders have a built-in pulser, which is employed as a check for the pulse counting of the scaler or rate meter. (The electric current has 60 cycles per second, or 3,600 per minute. Thus, the pulser should produce 3,600 counts per minute, if the scaler or rate meter is functioning properly.)

6. Reference Source. The pulser checks only the recorder. It is wise to have a gamma emitting source with a rather long half-life to also check on the proper operation and constancy of the detector. A tracer of antimony 125 (half-life, 2.7 yr.) or cobalt 60 (half-life, 5.4 yr.) is satisfactory. Also available is a mixture of barium 133 (half-life, 9.5 yr.) and cesium 137 (half-life, 33 yr.) in suitable proportions, so that their combined gamma-ray spectrum closely resembles that of I^{131}. This mixture is called "mock iodine" and is preferred only if one uses a scintillation spectrometer.

7. Body Background. Many investigators, including the authors, prefer to count the thigh for an estimate of body background. The lower thigh is approximately the same diameter as the neck and offers a more natural body background than that obtained by taking a reading over the thyroid area screened by a thick lead filter. In taking the thigh counts, especially in the sitting position, one is again cautioned of a detector that is poorly shielded from the side and its proximity to the thyroid.

8. Phantom. A cylinder of lucite is used to count the tracer to simulate the neck and produce a similar spectrum. Dr. Marshall Brucer of Oak Ridge, Tennessee, has found the ideal phantom to be a lucite cylinder 12.5 cm. in diameter and 12.5 cm. in height with an opening 2 cm. from the front and 7.5 cm. deep (for the tracer).

The use of a spectrometer or pulse analyzer has made the uptake procedure more complex and more accurate only from the physical standpoint. Thyroid uptakes performed with or without this added perfection have shown no difference that is clinically significant.

II. PHYSICAL FEATURES OF DIFFERENTIAL STUDIES

A differential study consists of a comparison of arbitrary counts, usually taken of identical points on each side. The rela-

TABLE I

FALL-OFF ALONG CENTRAL AXIS FROM ORIFICE

Cm.	Long Geiger-Müller Bismuth Tube	Short Geiger-Müller Bismuth Tube	Short Geiger-Müller Stainless Steel Tube	Scintillation Counter
	(Per Cent)	(Per Cent)	(Per Cent)	(Per Cent)
0	100	100	100	100
2	62	46	47	64
4	45	28	25	46
6	33	16	15	34
8	23	10	9	25

tive function of a thyroid nodule or metastatic site may be determined. Functioning substernal thyroid may be identified. The radioactive brain study procedure is actually a differential study, *i. e.*, comparison of identical points on each side of the skull.

The choice of the proper collimated detector is important in differential studies. If the fall-off from the detector is too rapid, any error in placing the detector, that is, not in contact with the body or at a slight angle, will lead to a considerable error in the reading. In Table 1, the fall-off along the central axis from the orifice of several collimated detectors is shown. Note the difference in the fall-off with the long bismuth Geiger-Müller tube and the scintillation counter, as compared with the two short tubes. The long Geiger-Müller tube and the scintillation counter that show a fall-off to 62 per cent and 64 per cent, respectively, in the first 2 cm. would be acceptable for differential readings, but the remaining two are not satisfactory.

The diameter of the opening of the collimator should not be too small or the detector would be critical to position. An opening of 2.5 to 3 cm. has been adequate in our studies. A larger opening may be used, being guided by the degree of localization desired.

In differential studies, the shielding of the crystal from the lateral side should be adequate. This is mandatory in taking differential counts in the presence of a high body background, such as one encounters in brain studies.

SUMMARY

The fundamental physical features of performing a thyroid uptake and differential study are presented. The adequate shielding of the crystal and the selection of a proper collimator are emphasized. The purpose of this paper is to summarize the basic physical information and make it readily available to the beginning operator in this field.

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THE EFFECT OF DISEASE AND DRUGS ON THE TWENTY-FOUR HOUR I^{131} THYROID UPTAKE

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THE performance of a twenty-four hour radioiodine (I^{131}) thyroid uptake test is technically simple. The answer is a definite number, the ratio between the amount of I^{131} administered and the amount concentrated in the thyroid gland. The interpretation of the meaning of this number is a medical task and is frequently not simple. In the interpretation of over 6,000 I^{131} tracer studies done in this department in the past ten years, we have encountered many problems. In this paper we will attempt to summarize the effect of (1) certain thyroid conditions, (2) certain systemic conditions, and (3) certain drugs and chemicals on the twenty-four hour I^{131} thyroid uptake.

This material has been assembled from the vast literature in this field and from our own experience.

THE TWENTY-FOUR HOUR I^{131} UPTAKE IN CERTAIN THYROID CONDITIONS (TABLE 1)

Euthyroidism. The twenty-four hour I^{131} thyroid uptake in euthyroidism is generally accepted to be between 15 per cent and 40 per cent. Values between 10 per cent and 15 per cent, and also between 40 per cent and 50 per cent may be found in clinically euthyroid individuals. When these values are encountered, additional studies such as thyroid suppression test, protein bound iodine (PBI), cholesterol, and basal metabolic rate (BMR) determinations are indicated and the evaluation of the clinical picture is of great importance. In some cases a therapeutic test with antithyroid medication may be desirable.

Hyperthyroidism. Uptakes over 50 per cent indicate an avidity of the thyroid gland for iodine. They are compatible with, but do not necessarily establish, a diagnosis of hyperthyroidism. In borderline values between 40 per cent and 50 per cent a thyroid suppression test is advisable, in which case a repeat I^{131} uptake study is done after the patient has received 3 grains of thyroid extract daily for ten days. In most euthyroids the I^{131} thyroid uptake will drop to 20 per cent or below; in hyperthyroid patients it will drop only slightly.

True hyperthyroidism results from excessive secretion of thyroid hormone into the circulation. It may occur without evidence of thyroid enlargement although it is usually associated with diffuse or nodular enlargement. "Hyperthyroidism without hypermetabolism" may exist, in which case the I^{131} thyroid uptake is high but the BMR and cholesterol values are normal. These patients show clinical improvement with I^{131} therapy and their I^{131} thyroid uptake returns to normal values. In "thyrotoxicosis factitia" I^{131} thyroid uptake values are normal or subnormal, while the patient exhibits the clinical picture of hyperthyroidism.

Hypothyroidism. Uptakes between 5 per cent and 15 per cent are compatible with, but do not establish a diagnosis of, hypothyroidism. Most factors interfering with the validity of the I^{131} uptake test decrease its value. When a low value is found which does not coincide with the clinical picture, it may take some careful investigation to elicit the interfering factor. Clinically, hypothyroid patients may show uptakes in the euthyroid range as described by Kurland and co-workers and termed "euthyroid hypometabolism." Values in the normal or hyperthyroid range may be found

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TABLE I

THE TWENTY-FOUR HOUR I^{131} THYRO UPTAKE IN CERTAIN THYROID CONDITIONS

Condition	I^{131} Thyr l Uptake Value		Clinical Observations
	Most Lik	Eventually	
Euthyroidism	15–40%		
Hyperthyroidism	over 50%		
Hypothyroidism	5–15%		
Myxedema	0–5%		
Thyrotoxicosis Factitia	N or D		Thyrotoxicosis
Genetic Hypothyroidism	N or H		Hypothyroidism
Euthyroid Hypometabolism	N		Hypothyroidism or myxedema
Hyperthyroidism without Hypermetabolism	H		Thyrotoxicosis but normal basal metabolic rate
Iodine Deficiency Goiter (colloid and nontoxic multinodular)	N or D	H or near 0	Goiter, hypothyroidism
Diffuse Exophthalmic Goiter	H		Diffuse goiter, hyperthyroidism, exophthalmos
Toxic Nodular Goiter	H or N		Hyperthyroidism
Struma Lymphomatosa (Hashimoto's disease)	L-N	D or H	Rapidly growing goiter, hypothyroidism, tenderness
Acute Thyroiditis	0 or D		Eu- or hypothyroidism
Invasive Fibrous Thyroiditis (Riedel's struma)	N or D		"Rock-hard" goiter, hypothyroidism
Granulomatous Thyroiditis (subacute thyroiditis)	D or 0	varies	Tenderness, perhaps toxic symptoms
Irradiated Thyroid (external radiation or radioiodine)	D or 0	may remain H, N or L-N	Clinical picture not always appropriate
Cretinism	H or N		Hypothyroidism
Neoplastic Goiters			
Adenoma	N	May be H	
Carcinoma	D or L-N		

Gradation: High (H). High-Normal (H-N). Normal (N). Low-Normal (L-N). Depressed (D). Zero (0).

in "genetic hypothyroidism" where an overactive thyroid produces a metabolically inactive hormone. A high I^{131} thyroid uptake may be found in hypothyroid patients for several weeks or longer after discontinuance of thyroid medication (rebound phenomenon). Eventually, the uptake gradually falls into the hypothyroid range.

Myxedema. Myxedema results from a prolonged lack of thyroid hormone. I^{131} uptakes from zero to 5 per cent are consistent with myxedema. Primary myxedema is caused by retrogressive changes in the thyroid gland itself. Pituitary myxedema results from insufficient thyroid stimulating hormone (TSH) production, usually the result of tumors or infarction in the anterior lobe of the hypophysis. Administration of exogenous TSH stimulates the thyroid to function in pituitary myxedema as indicated by an increased I^{131} thyroid uptake in twenty-four to forty-eight hours. In primary myxedema there is no response to TSH.

Iodine Deficiency Goiters. Endemic, simple, colloid or nontoxic multinodular goiters are frequently seen in endemic goiter areas in which the iodine intake by the population is low. They start as a simple enlargement at puberty and continue to grow, later undergoing retrogressive changes and becoming multinodular. They may reach huge sizes. Such goiters take up less iodine per gram but, because of their size, take up as much total iodine as a normal gland. Scanning shows the I^{131} uptake to be quite uneven. When retrogressive changes predominate, the I^{131} uptake may be low.

Usually it is in the low euthyroid range but it may also be in the hyperthyroid range indicating overactivity. This may occur without clinical signs or after many years, averaging 14.5 years according to Plummer, and results in thyrotoxicosis.

Diffuse Exophthalmic Goiter or Graves' Disease. Uptake values of 50 per cent or more are consistent with Graves' disease. The thyroid gland may be of normal size although usually there is a diffuse enlargement. Exophthalmos is commonly found. There is no correlation between the severity of the disease and the height of the I^{131} thyroid uptake, *i.e.*, a patient with an uptake of 90 per cent need not be extremely ill.

Toxic Nodular Goiter. An asymmetric nodular enlargement of the thyroid gland accompanied by symptoms of thyrotoxicosis generally indicates the presence of one or more toxic nodules. Usually exophthalmos is absent, the toxicity is less than in Graves' disease, and the I^{131} uptake is in the hyperthyroid range although patients have been seen who were quite ill with a normal uptake. In some cases this may be caused by previous iodine medication, since a nodular goiter eliminates iodine reluctantly whereas an exophthalmic goiter has a rapid turnover of iodine. Also, the active nodule may be small and located posteriorly. In the absence of a scanner, a spot scan can be made by counting with the counter, touching the skin over the nodule and comparing it with a count over a similar area on the opposite side. Usually the nodule has a count several times that of the rest of the gland.

Struma Lymphomatosa—Hashimoto's Disease. Uptake values between 5 per cent and 95 per cent have been reported in Hashimoto's disease.[43,145] Generally, uptakes in the normal or low-normal range are found. This disease is most common in women between forty and fifty-five years of age. The thyroid gland shows uniform bilateral enlargement which may have developed rapidly. A normal contour is maintained and the gland's consistency is firm. Histologically, there is a diffuse infiltration by lymphoid cells with associated atrophy of the thyroid parenchyma and a varying degree of interstitial fibrosis. The systemic symptoms depend on the amount of functioning thyroid tissue remaining.

Acute Thyroiditis. Extremely low uptake values are observed in every instance of acute thyroiditis. Clinically the patient may remain euthyroid or may become hypothyroid, depending upon the amount of destruction of the thyroid gland incident to the inflammatory process. Recovery usually takes place after one or more months when the I^{131} uptake test gradually indicates normal values. Several cases are reported in the literature in which hyperthyroidism developed immediately after, or up to eight months following, an episode of actue thyroiditis.

Invasive Fibrous Thyroiditis—Riedel's Struma. In Riedel's struma[176] there is replacement of the thyroid parenchyma by dense fibrous scar tissue. The hard consistency has given origin to the term "rock hard" thyroid. The gland is usually not greatly but uniformly enlarged. The I^{131} thyroid uptake in Riedel's struma may either be in the normal range or be depressed, depending upon the stage of the disease. Any marked functional disturbance is unusual and hypothyroidism is not commonly troublesome.

Granulomatous Thyroiditis—de Quervain's Thyroiditis. Granulomatous thyroiditis[177] apparently is a true nonsuppurative inflammation of the thyroid gland representing a distinct clinicopathologic entity. The disease has been reported under many synonyms and is best known as "subacute thyroiditis." The enlargement of the gland is moderate with tenderness, and the process is unilateral in 50 per cent of the cases. The I^{131} uptake is usually zero or markedly depressed although occasionally normal uptake values are found, especially if the test is performed in the healing phase. Cases have been reported which exhibited Graves' disease in addition to unilateral or focal granulomatous thyroiditis. The I^{131} uptakes in those cases were in the hyper-

thyroid range but directional counting over the areas of granulomatous thyroiditis revealed poor pick up of I^{131}. In some cases symptoms of toxicity were considered to be due to the release of excessive amounts of thyroid hormone into the circulation as a result of destruction of thyroid tissue by thyroiditis. A complication of this disease may be temporary or permanent hypothyroidism or myxedema.

Irradiated Thyroid. Irradiation of the thyroid, either by external rays or therapeutic I^{131}, will reduce the twenty-four hour uptake. The amount of reduction depends on dosage, the stage of activity of the gland at the time of irradiation, and the length of time hyperactivity has been present. Acute epithelial injury associated with necrotizing vasculitis and thrombosis is the initial lesion resulting from high doses of radiation. The late reaction is characterized by follicular atrophy accompanied by perifollicular fibrosis. Hyperplastic cells are more sensitive to radiation than normal cells and cells with a short history of hyperactivity appear to be more sensitive than cells with a long history.

Postsurgery Thyroid. Either after partial thyroidectomy or simple exploratory operation, the I^{131} thyroid uptake is temporarily depressed. This may be true even in the absence of reduced thyroid activity.

Cretinism. It has been noted that the thyroid gland of goitrous and nongoitrous cretins has an increased avidity for I^{131} as shown by an increased thyroid uptake rather than low thyroid activity as one might expect with this type of clinical picture. As possible explanations of this discrepancy are suggested first the inability of the thyroid gland to achieve the final synthesis of an active thyroid hormone due to an intrinsic, perhaps familial, defect of the gland. Iodine may be readily accumulated in those glands and even di-iodotyrosine and tri-iodotyrosine can be demonstrated by chromatography. Secondly, the existence of a "blocking mechanism" is thought of, similar to that observed in glands blocked by antithyroid drugs, where iodine cannot be converted into iodide. These observations again emphasize the danger of permitting laboratory tests to take precedence over clinical assessment of the patient, since of themselves they might readily be interpreted as indicating thyrotoxicosis.

THE TWENTY-FOUR I^{131} THYROID UPTAKE IN NEOPLASTIC GOITERS

Adenoma. An adenoma of the thyroid is a benign localized true epithelial neoplasm as distinguished from the nodular areas of localized hyperplasia and involution as seen in nodular goiters. Several histologic types are differentiated, such as papillary, colloid, fetal and embryonal adenoma and Hürthle cell tumor. Functional activity of thyroid adenomas seldom gives rise to metabolic disturbances in comparison to tumors of other endocrine organs. There is little evidence of significant amounts of hormone production by thyroid adenomas. While hyperthyroidism may be present with adenomas, it appears more often to be due to hyperplasia of some of the surrounding thyroid tissue rather than to hyperfunction of the adenoma itself. A differential study or scintigram should be made of a thyroid nodule to determine its relative function. A good functioning nodule is much more likely to be benign.

Carcinoma. The most frequent malignant neoplasm of the thyroid gland is carcinoma. A number of different histologic types of carcinoma are distinguished, including papillary carcinoma, alveolar or follicular carcinoma, giant cell carcinoma, small cell carcinoma, etc. Sarcomatous tumors of the thyroid gland are very rare, the most frequent being fibrosarcoma and lymphosarcoma. Carcinoma has never been demonstrated to concentrate I^{131} as avidly as normal thyroid tissue. This fact is of clinical usefulness in suggesting or confirming malignant neoplasm, but only in cases with additional strong clinical evidence of a malignancy. The finding of a low I^{131} uptake is merely consistent with neoplasm. The final diagnosis can only be obtained by biopsy. The height of the I^{131}

uptake will depend first upon how much normal thyroid tissue is replaced by tumor tissue and, secondly, upon the type of carcinoma present. The concentration of I^{131} by different histologic types of carcinoma is variable although generally low. Less than 50 per cent of carcinomas of the thyroid gland have been found to concentrate I^{131} in measurable amounts. Nevertheless, there are certain histologic types which pick up I^{131} quite avidly, especially at their metastatic sites. Generally, it has been concluded that colloid producing carcinoma will concentrate I^{131} sufficiently to justify subsequent treatment with I^{131}. Colloid production is found in alveolar or follicular carcinoma and less commonly in papillary carcinoma of the thyroid-gland. These are better differentiated and of low or moderate malignancy. They have a more favorable prognosis. None of the remaining types, such as giant cell carcinoma, small cell carcinoma, or other undifferentiated types, has ever shown sufficient I^{131} concentration to make I^{131} therapy reasonable. Differentiation of carcinoma from other thyroid disorders having low uptakes on the basis of an I^{131} thyroid uptake study alone is quite impossible.

THE TWENTY-FOUR HOUR I^{131} THYROID UPTAKE IN CERTAIN SYSTEMIC CONDITIONS AND EXTRATHYROID DISEASES (TABLE II)

Childhood. The twenty-four hour I^{131} thyroid uptake in 60 normal children ranged from 17 per cent to 50 per cent, with a mean of 31.1 ± 7.6 per cent as shown by Oliner and associates.[113] This range and mean value did not differ from a control study in 64 euthyroid adults. There did not appear to be any difference between boys and girls, nor was there any variation with age. No correlation between I^{131} uptake and body weight was noted. Uptake data on 5 hypothyroid children showed a range of 3 per cent to 15 per cent at twenty-four hours, whereas in 4 hyperthyroid children the range was from 72 per cent to 99 per cent. These observations indicate that the commonly used ranges for adults also apply to children.

Senescence. It has been recognized that some of the features of senescence are similar to those of the hypothyroid state. However, there is no convincing proof that secretion of thyroid hormone decreases with advancing age. Occasionally, in senile patients, the I^{131} thyroid uptake values are found to be in the low-normal or hypothyroid range which can only be explained as being due to senility.

Mongolism. Mongolism is believed to result from deceleration of normal growth during the fetal period. At Cook County Hospital, a study of 56 mongoloid children showed the twenty-four hour I^{131} thyroid uptake to be in the normal and low-normal range. This confirms reports of Kurland *et al.*,[81–83] and Cottino and co-workers.[26] The uptakes of 7 parents of mongoloid children were normal.

Pituitary Disease. It is reported, and our own experience confirms, that the twenty-four hour I^{131} thyroid uptake is in the normal range in most patients with pituitary tumors. After hypophysectomy uptakes fall to myxedema level in about four weeks.

Addison's Disease. The close association of the thyroid and adrenal cortex and the dependence of both organs on the function of the anterior pituitary are known, and one might be inclined to anticipate some type of thyroid dysfunction in Addison's disease. Ordinarily, the I^{131} uptake study in Addison's disease will show normal values, unless there is an effect of massive cortisone medication upon the thyroid function.

Liver Disease. Mueller *et al.*[109] studied a series of 49 patients exhibiting liver disease without evidence of thyroid disturbance. Twenty patients had an I^{131} thyroid uptake of 50 per cent or higher, associated most frequently with spider angiomata, jaundice, and microscopic evidence of severe cellular damage to the liver. In spite of the increased uptake in the presence of liver disease, no evidence of increased production of thyroid hormone could be discovered either clinically or by laboratory meth-

TABLE II

THE TWENTY-FOUR HOUR I^{131} THYROID UPTAKE IN CERTAIN SYSTEMIC CONDITIONS AND EXTRATHYROID DISEASES

Condition	I^{131} Thyroid Uptake Value		Clinical Observations
	Most Likely	Eventually	
Childhood			Adulthood values applicable
Mongolism	N or L-N		
Senescence	N or L-N	D	Senility
Pituitary Diseases			
Eosinophilic Tumor	N		
Acromegaly	N		
Chromophobic Tumor	L-N		
Basophilic Tumor	L-N	D	
Hypophysectomy	D or o		
Addison's Disease	N or L-N		
Liver Disease	H or N		
Renal Disease	H or N		
Congestive Heart Failure			
Uncomplicated	N		Complications such as thyrotoxicosis, renal or hepatic disorders
Complicated	H	D	
Pancreatic Insufficiency		D (?)	
Iodine Restricted Diet	H or N		High after three months on diet
Alcoholism	H		
Pregnancy	H or H-N		During last month
Menstruation	N		
Anorexia Nervosa	N or L-N	D	Low basal metabolic rate
Myotonic Dystrophy	N or L-N		
Hypothalamic Lesions	D		
Malignant Melanoma	N		
Leukemia	N		Hypermetabolism
Severe Stress	D		In rats
Acute Bleeding	o to L-N	L-N or N	

Gradation: High (H). High-Normal (H-N). Normal (N). Low-Normal (L-N). Depressed (D). Zero (o).

ods. Kidney function tests appeared to rule out possible renal disturbance as a cause of the elevated thyroid uptake. It is concluded that high I^{131} thyroid uptakes do occur in certain liver diseases under certain circumstances and may be misleading in patients with liver disease whose symptoms might require the exclusion of thyrotoxicosis.

Renal Disease. The twenty-four hour I^{131} thyroid uptake is not affected by renal disease. The forty-eight hour uptake may be elevated due to retained high levels of RAI in the blood stream.

Congestive Heart Failure. In uncomplicated congestive heart failure the BMR may be elevated and the serum cholesterol lowered. However, the twenty-four hour I^{131} uptake remains normal. Thyrotoxicosis may have led to the heart failure. The I^{131} uptake in those situations is naturally high. In other more complicated cases thyrotoxicosis may be present in addition to hepatic and renal insufficiency.

Pancreatic Insufficiency. The I^{131} uptake is low, not over 3 per cent, in patients with pancreatic insufficiency.

Iodine Restricted Diet. After a prolonged iodine deficient diet, there is likely to be a high I^{131} thyroid uptake.

Alcoholism. Alcoholic patients often show an elevated I^{131} thyroid uptake without clinical hyperthyroidism. A pre-existing dietary deficiency of iodine best explains the enhanced thyroid avidity for iodine in those cases. The gland is thought to be in a state of "starvation" and rapidly accumulates iodine.

Pregnancy and Menstruation. Thyroid I^{131}

uptakes during pregnancy have been found to be increased above normal by about 15 per cent during the last ten weeks of pregnancy and are definitely lower post partum. The twenty-four hour uptake does not vary detectably with the menstrual cycle.

Anorexia Nervosa. Although anorexia nervosa is primarily of psychologic origin, the existence of an endocrinologic deficiency has been periodically suggested. This has been prompted by the presence of amenorrhea and a low basal metabolic rate. The I^{131} thyroid uptake was found to be normal or within the low-normal range.

Myotonic Dystrophy. Patients with myotonic dystrophy customarily have low basal metabolic rates, but myxedema has rarely been observed. Enlargement of the thyroid gland has been repeatedly reported, but the precise incidence is unknown. I^{131} thyroid uptake studies show either normal, subnormal or myxedematous values.

Malignant Melanoma. Kory *et al.*[78] showed that in no case was there any evidence of selective I^{131} uptake by tumor tissue of malignant melanoma. This observation eliminates this disease from being a possible source of error in the interpretation of the I^{131} thyroid uptake test.

Leukemia. In a small clinical series, Albright and Middleton[1] could not demonstrate any alteration of the I^{131} thyroid uptake in leukemic patients although the basal metabolic rate was elevated. They considered the regularity of the results as sufficient direct evidence of nonparticipation of the thyroid gland in the elevated metabolism in leukemic patients.

Acute Bleeding. During recent years at Cook County Hospital, attention has been paid to variations of the thyroid uptake of I^{131} in acutely bleeding patients. Routine thyroid uptake tests in 38 female patients with vaginal bleeding, such as functional disorders, menorrhagia and metrorrhagia, or massive bleeding due to malignant growth showed the I^{131} thyroid uptake values ranging between zero and 25 per cent with an average of 13 per cent. The uptake studies were performed during the active state of the bleeding. All other possible interfering mechanisms had been excluded. In most instances the tests were repeated after the bleeding had stopped and the values were found to have climbed considerably, being then within the low-normal or normal range. Isolated cases of severe rectal and upper gastrointestinal tract bleeding also showed markedly depressed thyroid uptake values which returned to normal after cessation of the bleeding.

CHEMICALS AND DRUGS INFLUENCING THE TWENTY-FOUR HOUR I^{131} THYROID UPTAKE (TABLE III)

The ingestion of excessive amounts of I^{127} (over 1–2 mg.) will markedly depress the twenty-four hour I^{131} thyroid uptake, often to zero value. The iodine found in the average diet, including iodized salt and some iodine-containing multivitamin preparations, does not seem to interfere. Practically all of the other iodine-containing medications invalidate the study for a period of time, depending upon the type of goiter and form of medication. For example, the I^{131} uptake of a diffuse toxic goiter may be valid in one week after cessation of Lugol's solution, but the I^{131} uptake of a toxic nodular goiter may be depressed for many months. The time required for a normal thyroid to show a valid I^{131} uptake will vary between these two extremes. The period during which one gets an invalidated I^{131} uptake does not seem to depend on the duration of I^{127} treatment. There are innumerable iodine preparations on the market. Many trade names do not refer to their iodine content (Table IV). Cough syrups, preparations for symptomatic treatment of asthma, certain vaginal suppositories, skin ointments and substances used in dental procedures all may have a sufficiently strong iodine component to interfere with the I^{131} thyroid uptake test. If a doubtful uptake results in a patient that has had a drug, the content of which is not completely known, a pharmacopoeia should be consulted. Iodine containing dyes used as contrast media in diagnostic radiology may depress the I^{131} thyroid uptake for a variable length of time.

TABLE III

CHEMICALS AND DRUGS THAT INTERFERE WITH TWENTY-FOUR HOUR I^{131} THYROID UPTAKE

A. *Iodine Containing Compounds*

These drugs all depress the twenty-four hour uptake but vary in degree depending upon the type of thyroid. In general, the interference is usually longer with euthyroid patients and nodular goiters and much shorter with diffuse exophthalmic goiters. The average interval of depression is given.

General Preparations (1–3 weeks):

Lugol's solution
Iodides
Antitussives
Iodine ointments (topical)
Iodine tincture (topical)
Iodoform (topical
Iodine suppositories
Vitamin preparations (occasional)
Enterovioform
Diodoquin
Enterosept
Neo-penil (Penicillin)

Contrast Media:

Aqueous Solutions
Diodrast (1–3 months)
Hypaque, Mediopaque, Neo-iopax, Urokon, Miokon, Thixokon, Renographin (1–2 weeks)
Dionosil (British) (2–4 months)
Oily Solutions (up to 1 year or more)
Lipiodol, Visciodol, Ethiodol, Iodochloral, Pantopaque
Cholecystopaques and Cholangiopaques
Cholografin (3 months), Telepaque (2 months), Priodax (1–3 months)
Uterosalpingopaques
Skiodan acacia, Salpix (1 month)

B. *Other Chemicals and Drugs*

These preparations all depress the twenty-four hour I^{131} thyroid uptake, usually less and for a shorter time in hyperthyroidism. The average interval of depression is given when known.

Antithyroid Drugs (2–8 days):
Thiouracil, Propylthiouracil, Methylthiouracil, Iothiouracil (Itrumil), Muracil, Methimazole (Tapazole), Mercazole, Carbimazole
Thyroid Medication (1–2 weeks)
Desiccated thyroid, Thyronine, Thyroxine, Thyroglobuline
Thiocyanates (1 week)
Perchlorate (1 week)
Nitrate
Sulfonamides (1 week)
Orinase
Progesterone
Adrenal Cortical Steroids (1 week or less)
Cortisone, Corticosterone, Desoxycorticosterone, Prednisone, Prednisolene
ACTH
Resorcinol
Cobalt (1 week or less)
PAS and Isoniacid (1 week after prolonged use)
Butazolidin
Amphenone (2–3 days)
Antihistamines (1 week or less)
Phenothiazine
Pentothal (1 week)

C. *Compounds that Enhance the Twenty-four Hour I^{131} Thyroid Uptake*

Thyroid Stimulating Hormone (TSH)
Estrogens (not persistently)

TABLE IV

VARIOUS IODINE PREPARATIONS THE NAMES OF WHICH DO NOT REFER TO THE IODINE CONTENT

Amend's solution	Entodon
Arocalcin	Limodin
Calathesin	Organidin
Calcidin	Quin-O-Creme
Ceradine	Tamponets
Child's Drikof	Thyractin
Endoarsan	Felsol

Antithyroid Drugs. Thiourea derivatives, such as thiouracil, propylthiouracil, methylthiouracil, iothiouracil (itrumil) and nuracil depress the formation of thyroxine. Iodide is rapidly concentrated in the cell but synthesis to thyroxine is blocked.

Since the iodine concentrating power of the thyroid gland is not influenced during the initial few hours following administration, the two hour I^{131} uptake is not altered, showing a "falsely" normal uptake. However, the follicular cells will soon be oversaturated with iodine and no further concentration takes place. The twenty-four hour uptake of iodine then becomes lower. The initially excessively accumulated iodine is released from the follicular cell back into the blood stream. When thiourea derivatives are discontinued, the enzymes recover in the relatively short period of six to forty-eight hours. With recovery, there is an increased rate of uptake due to "starvation" of the gland which is known as "rebound phenomenon." This phenomenon may be lacking in patients with hyperplastic thyroid tissue but can usually be observed with normally functioning thyroid tissue. A chemically different group of antithyroid drugs—methimazole (tapazole), mercazole and carbimazole—seems to act quite similarly to the thioureas. The twenty-four hour I^{131} thyroid uptake is markedly inhibited. The suppression in normal human subjects lasts slightly longer with neomercazole than after mercazole medication. In summary, one can state that the twenty-four hour I^{131} thyroid uptake is depressed during the administration of thiourea derivatives in euthyroid as well as in hyperthyroid patients. The same is true for other antithyroid drugs, such as methimazole, mercazole and carbimazole. There is a rapid recovery with the values returning to normal within two to eight days.

Thyroid Medication. The ingestion of thyroid substance decreases the function of the thyroid gland primarily through pituitary inhibition. Thyroid function returns to normal in most patients within two weeks. Some show depression up to six to eleven weeks. In a few patients there may be a "rebound phenomenon," with the I^{131} thyroid uptake being higher than before medication. The uptake in toxic adenomatous and exophthalmic goiter cannot be depressed to hypothyroid levels by even large quantities of desiccated thyroid. This disparity of the effect of thyroid medication in normal and in hyperthyroid patients is utilized as a differential test in borderline cases. There is apparently no difference in response of patients to thyroxine and to thyroid extract. Synthetic thyroxine offers the advantage of uniform strength and composition and greater stability.

Thyroid Stimulating Hormone (TSH). TSH increases the I^{131} uptake by the thyroid gland, except in primary thyroid myxedema. The effect is found to be more marked in euthyroid than in hyperthyroid patients. The uptakes will be successively higher as the gland depletes its store of iodine.

Sulfonamides. Sulfonamides belong to the aminobenzene group which includes para-aminosalicylic acid and para-aminobenzoic acid. The aminobenzenes act similarly to the thiourea derivatives, lowering the I^{131} thyroid uptake. Recovery is rapid, and proper uptake studies can be performed in one week following cessation of medication. Orinase acts in the same manner.

Thiocyanate, Perchlorate, Nitrate. Potassium and sodium thiocyanate in doses of 1 or 2 mg. orally or intravenously result in loss of the concentrating ability of the follicular cell membrane. Thus the I^{131} thyroid uptake studies during this medication are markedly depressed. Thiocyanates are rap-

idly removed from the blood stream and excreted. Normal uptake tests can be performed after a two to three day interval and certainly after one week. Similar action upon the follicular cell was found to be caused by other monovalent anions; such as nitrates and perchlorates. Perchlorate is more potent in preventing the uptake of a tracer than iodine, nitrate and thiocyanate. In summary, thiocyanate, perchlorate and nitrate should be considered as potently depressing the I^{131} thyroid uptake in euthyroidism and hyperthyroidism.

Gonadal Hormones. The effect of gonadal hormones upon the I^{131} thyroid uptake has been investigated in animal and human experiments. In our experience at the Cook County Hospital, no consistent significant influence has been found.

Adrenal Cortical Steroids and Stress. The inhibitory effect of adrenal cortical steroids on thyroid function is quite well established although there is no entire agreement as to the mechanism of action. The twenty-four hour I^{131} thyroid uptake is markedly depressed following the administration of corticotrophin, cortisone, prednisone, prednisolene and ACTH. With daily doses of cortisone below 100 mg., very little effect was noted on thyroid function.

Resorcinol. Resorcinol ointments are in common use in dermatology. Three cases of definite myxedema as indicated by clinical and laboratory means have been reported by Bull and Fraser,[18] occurring in elderly women following prolonged application of a resorcinol ointment to varicose ulcers. Subsequent experimental studies of the effect of resorcinol on the I^{131} thyroid uptake in rats confirmed the clinical observations. There was maximal depression of the iodine accumulation. The action of resorcinol upon the thyroid is suggested to be similar to that of thiourea derivatives.

Cobalt Medication. Profoundly depressed I^{131} thyroid uptakes have been observed in isolated cases following cobalt medication.

Para-aminosalicylic Acid (PAS) and Isoniacid. Clinical observations have indicated that goiter, transient hypothyroidism and myxedema may occur as a complication in a few patients treated with PAS for tuberculosis over prolonged periods of time, six months or more. Avid uptakes have been observed after withdrawal of the drug. *In vitro* tests have indicated that isoniacid also exerts an antithyroid effect but even weaker than para-aminosalicylic acid.

Tranquilizing Agents. The effect of tranquilizing agents upon the thyroid uptake was investigated by Friedell[42] in patients who showed an elevated I^{131} uptake but were without clinical signs of hyperthyroidism. Drugs employed were meprobamate (Miltown) and meprobamate fortified with benactyzine hydrochloride. The initial I^{131} thyroid uptakes varied from 35 per cent to 62 per cent. Tranquilizing agents, particularly meprobamate fortified with benactyzine, reduced the uptake to below 30 per cent in most instances. One patient failed to respond to the drugs and the diagnosis of true hyperthyroidism was subsequently established in this case. The effect upon the I^{131} thyroid uptake is thought to be via the central nervous system. Tranquilizing agents do not have any effect upon the I^{131} thyroid uptake in the presence of true hyperthyroidism.

Antihistamines. Recently antihistamines have come into common use in a broad field of indications. Occasionally, they are administered over prolonged periods of time. At Cook County Hospital the interference of these drugs upon the thyroid uptake of iodine has been noted for several years. We have recently performed a clinical study to evaluate the importance of this interference. Fifty euthyroid patients and 12 hyperthyroid patients, mainly representing cases in which a routine I^{131} uptake test was requested, were given antihistamines for one week and the test was repeated on the last day of medication. Chlortrimeton was used in 51 cases and dimetane in 9 cases. One tablet of 4 mg. of chlortrimeton or dimetane was administered four times daily for seven days. The total dosage varied slightly between 100 and 110 mg.

The results were as follow: In the *euthyroid* group (1) the twenty-four hour I^{131} thyroid uptake was reduced 20 per cent to 85 per cent in one-half of the cases. The average reduction was 52 per cent of the original uptake value. In one quarter of these cases the uptake dropped into the hypothyroid range although none of them reached zero. (2) The I^{131} thyroid uptake values before and after medication were within a range of $\pm$ 20 per cent in approximately one-half of the cases. This wide range is chosen on purpose in order to evaluate a wide range of errors. (3) A significant rise of the I^{131} thyroid uptake was observed in 2 cases. One of them was unexplainable. In the second case there was questionable iodine medication in the past and the test was probably performed during the recovery period of the gland. The observed values suited this explanation. In the *hyperthyroid* group (12 patients) (1) the I^{131} thyroid uptake was reduced from 20 per cent to 65 per cent with an average of 40 per cent in 8 of 12 patients. While the values dropped into the upper euthyroid range, there was no evidence of any change of the clinical picture. (2) No essential depressing effect was noted in the remaining 4 cases. Antihistamines moderately suppress the I^{131} thyroid uptake in some euthyroid as well as hyperthyroid subjects. Previous clinical observations have shown the recovery rate of the thyroid to be rapid, and true uptake values can be obtained after one week or less following cessation of medication. The possibility of the antihistamines acting as the interfering drug in unexplained low I^{131} thyroid uptakes is justified and should be considered.

Food. While beets, spinach, lettuce, cabbage, rutabaga, turnips, beans, peas, carrots, celery, strawberries, peaches, pears, peanuts, filberts, walnuts, oysters and clams are known to be goitrogenic, the usual quantities of these foods normally ingested have no significant effect on the twenty-four hour I^{131} thyroid uptake.

Pentothal. Anesthetic agents containing a thiocarbamate structure, *i.e.*, sodium 5-allyl-5-(1 methylbutyl) 2-thiobarbiturate (surital), sodium ethyl(1-methylbutyl)-thio barbiturate (thiopental) and pentothal inhibit thyroid activity immediately following administration, primarily by depriving the thyroid of available iodine. The inhibition of the thyroid activity may be prolonged from six to seven days.

TABLE V

INVESTIGATED CHEMICALS SHOWING NO INFLUENCE UPON THE TWENTY-FOUR HOUR I^{131} THYROID UPTAKE IN MAN

Fluorine	Aureomycin
Dinitrophenol	Penicillin
Reserpine	Calcium
Mercurials (?)	Testosterone (?)

Mercurials. Spies[151] determined that mercuhydrin had no effect upon the twenty-four hour I^{131} thyroid uptake in 8 euthyroid patients. Radioiodine clearances remained unchanged in the face of a consistent and marked increase in chloride excretion (Table v). The doses given were 2 ml. of mercuhydrin. In our experience diuretics used at the time of study may depress the I^{131} thyroid uptake; however, if the study is done after prolonged diuresis, the uptake may be elevated.

Antibiotics. Clinical observations at Cook County Hospital have not shown any remarkable effect of antibiotics upon the I^{131} thyroid uptake, although routine uptake studies on patients on antibiotic medication for varying lengths of time were done (Table v). There is one iodine-containing penicillin on the market, penethamate hydriodide (neo-penil) which has been shown to interfere with the protein-bound iodine determination as a test of thyroid function. It may be anticipated, that neo-penil will also interfere with the I^{131} thyroid uptake.

SUMMARY

1. The results of the twenty-four hour thyroid uptake of I^{131} in various thyroid diseases have been summarized. This has been attempted in order to provide a rapid and convenient guide for optimal interpre-

tation of the test, especially in controversial appearing situations.

2. A fact-finding survey has been made of certain systemic conditions or diseases and chemical substances which do or might possibly interfere with the performance of the I^{131} thyroid uptake test. We have tried to present comprehensively practically all conditions or substances which have been proved to interfere with the uptake studies. At the same time a number of drugs and situations are cited in which the eventuality of interference exists, suggested on the basis of animal experiments or theoretic clinical considerations.

3. From the findings we have demonstrated that the twenty-four hour I^{131} thyroid uptake has diagnostic usefulness only when the results are properly interpreted in conjunction with other clinical and laboratory findings. It has not replaced sound clinical judgment.

4. In conclusion, the purpose of the paper is to present the fundamental concepts of I^{131} thyroid uptakes, as obtained from the experience of the authors and the review of the vast amount of literature available, in one single paper to make it a convenient working reference.

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REFERENCES

1. ALBRIGHT, E. C., and MIDDLETON, W. S. Uptake of radioactive iodine by thyroid gland of leukemic patients. *Blood*, 1950, *5*, 764–766.
2. ASTWOOD, E. B., GREER, M. A., and ETTLINGER, M. G. Antithyroid factor of yellow turnip. *Science*, 1949, *109*, 631.
3. ASTWOOD, E. B. Mechanism of action of various antithyroid compounds. *Ann. New York Acad. Sc.*, 1944, *50*, 419–443.
4. ASTWOOD, E. B., SULLIVAN, J., BISSELL, A., and TYSLOWITZ, R. Action of certain sulfonamides and of thiourea upon function of thyroid gland of rat. *Endocrinology*, 1934, *32*, 210–225.
5. BALINT, J. A., FRASER, R., and HANNO, M. G. W. Radio-iodine measurements of thyroid function during and after P.A.S. treatment of tuberculosis. *Brit. M. J.*, 1954, *1*, 1234–1237.
6. BARTELS, E. C., and SJORGREN, R. W. 1-methyl-2-mercaptoimidazole: New active antithyroid agent. *J. Clin. Endocrinol.*, 1951, *11*, 1057–1062.
7. BEIERWALTES, W. H., JOHNSON, P. C., and SOLARI, A. J. Clinical Use of Radioisotopes. W. B. Saunders Company, Philadelphia, 1957.
8. BEIERWALTES, W. H. Value of radioactive iodine uptake and protein-bound iodine estimations in diagnosis of thyrotoxicosis. *Ann. Int. Med.*, 1956, *44*, 40–51.
9. BEIERWALTES, W. H. 1-methyl-2-mercaptoimidazole and 1-ethyl-2-mercaptoimidazole: Clinical evaluation of two new antithyroid drugs. *J. Lab. & Clin. Med.*, 1950, *36*, 861–865.
10. BERSON, S. A., and YALOW, R. S. Effect of cortisone on iodine accumulating function of thyroid gland in euthyroid subjects. *J. Clin. Endocrinol. & Metabol.*, 1952, *12*, 407–422.
11. BISHOPRIC, G. A., GARRETT, N. H., and NICHOLSON, W. M. Thyroidal uptake of radioactive iodine as modified by iodine restricted diet. *J. Clin. Endocrinol. & Metabol.*, 1955, *15*, 593–597.
12. BLISS, E. L., and MIGEON, C. J. Endocrinology of anorexia nervosa. *J. Clin. Endocrinol. & Metabol.*, 1957, *17*, 766–776.
13. BLOODWORTH, J. M. B., JR., KIRKENDALL, W. M., and CARR, T. L. Addison's disease associated with thyroid insufficiency and atrophy (Schmidt syndrome). *J. Clin. Endocrinol. & Metabol.*, 1954, *14*, 540–553.
14. BÖE, J., and GABRIELSEN, Z. Antithyroid drugs plus roentgen irradiation in treatment of hyperthyroidism. *J. Clin. Endocrinol. & Metabol.*, 1954, *14*, 939–947.
15. BOGOROCH, R., and TIMIRAS, P. Response of thyroid gland of rat to severe stress. *Endocrinology*, 1951, *49*, 548–556.
16. BOTKIN, A. L., and TEW, J. T. Thyroid and adrenal response to varying dose levels of epinephrine. *Proc. Soc. Exper. Biol. & Med.*, 1952, *79*, 378–379.
17. BRADLEY, W. O. Effects of certain antithyroid drugs on uptake of radioactive iodine by frog thyroid. *Biol. Bull.*, 1951, *101*, 62–70.
18. BULL, G. M., and FRASER, R. Myxedema from resorcinol ointment applied to leg ulcers. *Lancet*, 1950, *1*, 851–855.
19. CALESNICK, B., HARRIS, W. D., and JONES, R. S. Antithyroid action of antibiotics. *Science*, 1954, *119*, 128–129.
20. CASTOR, C. W., and BEIERWALTES, W. H. Effect of 2,4-dinitrophenol on thyroid function

in man. *J. Clin. Endocrinol. & Metabol.*, 1956, *16*, 1026–1031.

21. Chapman, E. M., and Maloof, F. Use of radioactive iodine in diagnosis and treatment of hyperthyroidism: 10 years' experience. *Medicine*, 1955, *34*, 261–321.
22. Chapman, E. M., Maloof, F., Maisterrena, J., and Martin, J. M. Ten years' experience with radioactive iodide. *J. Clin. Endocrinol. & Metabol.*, 1954, *14*, 45–55.
23. Chevalley, J., McGavack, T. H., Kenigsberg, S., and Pearson, S. Four-year study of treatment of hyperthyroidism with methimazole. *J. Clin. Endocrinol. & Metabol.*, 1954, *14*, 948–960.
24. Chinn, A. B., Lavik, P. S., Babb, L. I., Buckaloo, G. W., Stitt, R. M., and Abbott, W. E. Blood isotope levels following test meal of I^{131}-labeled protein. *J. Lab. & Clin. Med.*, 1953, *42*, 377–379.
25. Clark, R. E., and Shipley, R. A. Thyroidal uptake of I^{131} after iopanoic acid (telepaque in 74 subjects). Letter to editor. *J. Clin. Endocrinol. & Metabol.*, 1957, *17*, 1008–1010.
26. Cottino, F., Ferraris, G. M., and Coda, G. Thyroid function in mongolism. Letter to editor. *J. Clin. Endocrinol. & Metabol.*, 1956, *16*, 830–831.
27. Czerniak, P., and Harell-Steinberg, A. Chronology of events in development of subacute thyroiditis, studied by radioactive iodine. *J. Clin. Endocrinol. & Metabol.*, 1957, *17*, 1448–1453.
28. DiGeorge, M., and Paschkis, K. E. Sporadic hypothyroidism associated with goiter. *J. Clin. Endocrinol. & Metabol.*, 1957, *17*, 645–653.
29. Dobyns, B. M., Vickery, A., Maloof, F., and Chapman, E. M. Functional and histologic effects of therapeutic doses of I^{131} on thyroid in man. *J. Clin. Endocrinol.*, 1953, *13*, 548–552.
30. Doniach, I., and Fraser, R. Effect of resorcinol on thyroidal gland uptake of I^{131} in rats. *Lancet*, 1950, *1*, 855–856.
31. Dowling, J. T., Freinkel, N., and Ingbar, S. H. Effect of diethylstilbesterol on binding of thyroxine in serum. *J. Clin. Endocrinol. & Metabol.*, 1956, *16*, 1491–1506.
32. Dowling, J. T., Freinkel, N., and Ingbar, S. H. Thyroxine-binding by sera of pregnant women. Letter to editor. *J. Clin. Endocrinol. & Metabol.*, 1956, *16*, 280–281.
33. Emanuel, R. W. Endocrine activity in anorexia nervosa. *J. Clin. Endocrinol. & Metabol.*, 1956, *16*, 801–816.
34. Engstrom, W. W., and Markardt, B. Influence of estrogen on thyroid function. *J. Clin. Endocrinol. & Metabol.*, 1954, *14*, 215–222.
35. Epstein, D., Cantarow, A., Friedler, G., and Paschkis, K. E. Inhibition of thyroid function by cortisone and ACTH in hypophysectomized rats. *Proc. Soc. Exper. Biol. & Med.*, 1953, *82*, 50–53.
36. Feldman, J. D. Effect of estrus and estrogen on thyroid uptake of I^{131} in rats. *Endocrinology*, 1956, *58*, 327–337.
37. Fields, T., and Seed, L. Clinical Use of Radioactive Isotopes. The Year Book Publishers, Inc., Chicago, 1957.
38. Fraser, T. R., Garrod, O., Hanno, M. G. W., and Jadresic, A. Antithyroid activity and toxicity of mercazole and neo-mercazole. *J. Clin. Endocrinol. & Metabol.*, 1954, *14*, 1230–1244.
39. Frederickson, D. S., Ganong, W. F., and Hume, D. M. Thyroid uptake of radioactive iodine in dog; effect of diet, hypophysectomy, and TSH. *Proc. Soc. Exper. Biol. & Med.*, 1955, *89*, 416–419.
40. Freinkel, N., and Ingbar, S. H. Relationship between metabolic activity and iodine-concentrating capacity of surviving thyroid slices. *J. Clin. Endocrinol. & Metabol.*, 1955, *15*, 442–458.
41. Freinkel, N., and Ingbar, S. H. Effect of metabolic inhibitors upon iodine transport in sheep thyroid slices. *J. Clin. Endocrinol. & Metabol.*, 1955, *15*, 598–615.
42. Friedell, M. T. Effect of tranquilizing agents on radioactive iodine uptake in thyroid gland. *J.A.M.A.*, 1958, *167*, 983–984.
43. Furr, W. E., Jr., and Crile, G., Jr. Struma lymphomatosa: Clinical manifestations and response to therapy. *J. Clin. Endocrinol. & Metabol.*, 1954, *14*, 79–86.
44. Ganong, W. F., Frederickson, D. S., and Hume, D. M. Depression of thyroidal iodine uptake by hypothalamic lesions. *J. Clin. Endocrinol. & Metabol.*, 1954, 14, 773–774. (Abstr.)
45. Gassner, F. X., Hopwood, M. L., Herrold, E. A., and Plummer, A. J. Interpretation of goitrogenic properties of certain "antithyroid" agents. *J. Clin. Endocrinol.*, 1950, *10*, 1485–1498.
46. Godley, A. F., and Stanbury, J. B. Preliminary experience in treatment of hyperthyroidism with potassium perchlorate. *J. Clin. Endocrinol. & Metabol.*, 1954, *14*, 70–78.
47. Goldberg, R. C., Greep, R. O., and Nay, L. B., Jr. Modification of thyroid activity in absence of anterior pituitary gland. *Proc. Soc. Exper. Biol. & Med.*, 1953, *84*, 621–624.
48. Goldberg, R. C., Wolff, J., and Greep, R. O. Mechanism of depression of plasma protein bound iodine by 2, 4 dinitrophenol. *Endocrinology*, 1955, *56*, 560–566.
49. Goldsmith, R. E., and Eisele, M. L. Effect of

iodide on release of thyroid hormone in hyperthyroidism. *J. Clin. Endocrinol. & Metabol.*, 1956, *16*, 130–137.

50. GOLDSMITH, R. Experience with radioiodine tracer test in radioiodine-treated thyrotoxic patients. *Am. J. M. Sc.*, 1954, *227*, 403–407.
51. GOODMAN, J. R., FLORSHEIM, W. H., and TEMPEREAU, C. E. Resperine and thyroid function. *Proc. Soc. Exper. Biol. & Med.*, 1955, *90*, 196–198.
52. GRANT, W. C. Aureomycin and thyroid gland. *Science*, 1954, *120*, 724–725.
53. GREEN, T. W., WHITE, W. E., ENGELMAN, E. P., and KRUPP, M. A. Effect of butazolidin on I^{131} uptake by thyroid gland. *Proc. Soc. Exper. Biol. & Med.*, 1953, *82*, 155–157.
54. GREER, M. A., and SMITH, G. E. Method for increasing accuracy of radiodine uptake as test for thyroid function by use of desiccated thyroid. *J. Clin. Endocrinol. & Metabol.*, 1954, *14*, 1374–1384.
55. GREER, M. A. Role of hypothalamus in control of thyroid function. *J. Clin. Endocrinol. & Metabol.*, 1952, *12*, 1259–1268.
56. GREER, M. A., and ASTWOOD, E. S. Antithyroid effect of certain foods in man as determined with radioactive iodine. *Endocrinology*, 1948, *43*, 105–119.
57. GRIBETZ, D., TALBOT, N. B., and CRAWFORD, J. D. Goiter due to lymphocytic thyroiditis (Hashimoto's struma); its occurrence in preadolescent and adolescent girls. *New England J. Med.*, 1954, *250*, 555–557.
58. HAMILTON, H. B., and WERNER, S. C. Effects of sodium iodide, 6-propylthiouracil, and 1-methyl-2-mercaptoimidazole during radioiodine therapy of hyperthyroidism. *J. Clin. Endocrinol.*, 1952, *12*, 1083–1084.
59. HAMOLSKY, M. W., GIERLACH, Z. S., and JENSEN, H. Uptake and conversion of radioactive iodine (I^{131}) by thyroid gland in vivo and in vitro in tourniquet shock in rats. *Am. J. Physiol.*, 1951, *164*, 35–43.
60. HANNGREN, A. Determination of antithyroid action of para-aminosalicylic acid using radioactive iodine; preliminary communication. *Lancet*, 1952, *2*, 117.
61. HERTZ, R., PITTMAN, J. A., and GRAFF, M. M. Amphenone: Toxicity and effects on adrenal and thyroid function in man. *J. Clin. Endocrinol. & Metabol.*, 1956, *16*, 705–723.
62. HERTZ, R., ALLEN, M. J., and TULLNER, W. W. Effects of amphenone "B" on thyroid, adrenals and genital tract of female rat. *Proc. Soc. Exper. Biol. & Med.*, 1950, *75*, 627–630.
63. HIGHLEY, D. R., and PARKER, H. E. Effects of liver fractions on thyroid function of rat. *Proc. Soc. Exper. Biol. & Med.*, 1955, *90*, 638–640.
64. HILL, S. R., JR., REISS, R. S., FORSHAM, P. H., and THORN, G. W. Effect of adrenocorticotropin and cortisone on thyroid function: Thyroid-adrenocortical relationships. *J. Clin. Endocrinol.* 1950, *10*, 1375–1400.
65. HOGNESS, J. R., WILLIAMS, R. H., and LANCE, M. Effect of amphenone "B" on adrenal, thyroid and testes. *Proc. Soc. Exper. Biol. & Med.*, 1952, *79*, 43–46.
66. HUBBLE, D. Familial cretinism. *Lancet*, 1953, *1*, 1112–1117.
67. HUTCHISON, J. H., and MCGIRR, E. M. Hypothyroidism as inborn error of metabolism. *J. Clin. Endocrinol. & Metabol.*, 1954, *14*, 869–886.
68. HURSH, J. B., VAN VALKENBURG, P. A., and MOHNEY, J. B. Effect of roentgen irradiation on thyroid function in rats. *Radiology*, 1951, *57*, 411–418.
69. HYDOVITZ, J. D., and ARONS, W. L. Effect of thyrotropin on pattern of thyroid hormones in plasma. *J. Clin. Endocrinol. & Metabol.*, 1957, *17*, 1332–1346.
70. INGBAR, S. H. Influence of single doses of propylthiouracil on kinetics of iodine accumulation by thyroid glands of normal and hyperthyroid subjects. *J. Clin. Endocrinol. & Metabol.*, 1955, *15*, 331–342.
71. JAIMET, C. H., and THODE, H. G. Thyroid function studies on children receiving cobalt therapy. *J.A.M.A.*, 1955, *158*, 1353–1355.
72. KEATING, F. R., JR. HAINES, S. F., POWER, M. H., and WILLIAMS, M. M. D. Radioiodine accumulating fuction of human thyroid gland as diagnostic test in clinical medicine. *J. Clin. Endocrinol.*, 1950, *10*, 1425–1464.
73. KEITEL, H. G., and SHERER, M. G. Marked depression of plasma protein-bound iodine concentration in absence of clinical hypothyroidism during testosterone medication. *J. Clin. Endocrinol. & Metabol.*, 1957, *17*, 854–861.
74. KIRKLAND, R. H. Impaired organic binding of radioiodine by thyroid following radioiodine treatment of hyperthyroidism. *J. Clin. Endocrinol. & Metabol.*, 1954, *14*, 565–571.
75. KLEIN, F., OTTIS, V., and VELVART, J. Myxoedema from resorcinol ointment applied to leg ulcers. Letter to editor. *Lancet*, 1950, *2*, 768.
76. KOHN, L. A., and NICHOLS, E. B. Interference with uptake of radioiodine tracer during administration of vitamin-mineral mixtures. *New England J. Med.*, 1955, *253*, 286–287.
77. KOMROWER, G. M. Case of myxedema developing during p-aminosalicylic acid therapy. *Brit. M. J.*, 1951, *2*, 1193–1194.
78. KORY, R. C., TUCKER, R. G., and MENEELY, G. R. Radioactive iodine in malignant melanoma. AM. J. ROENTGENOL., RAD. THERAPY & NUCLEAR MED., 1954, *72*, 119–123.

79. Kriss, J. P., Carnes, W. H., Gross, R. T. Hypothyroidism and thyroid hyperplasia in patients treated with cobalt. *J.A.M.A.*, 1955, *157*, 117–121.

80. Krosnick, A., Segal, H. I., and Israel, H. L. Penethamate hydriodide (neo-penil): Influence on blood protein-bound levels. *J. Clin. Endocrinol. & Metabol.*, 1954, *14*, 242–243.

81. Kurland, G. S., Fishman, J., Hamolsky, M. W., and Freedberg, A. S. Radioisotope study of thyroid function in 21 mongoloid subjects, including observations in 7 parents. *J. Clin. Endocrinol. & Metabol.*, 1957, *17*, 552–560.

82. Kurland, G. S., Hamolsky, M. W., and Freedberg, A. S. Studies in non-myxedematous hypometabolism; clinical syndrome and effects of triiodothyronine, alone or combined with thyroxine. *J. Clin. Endocrinol. & Metabol.*, 1955, *15*, 1354–1366.

83. Kurland, G. S., Freedberg, A. S., and Fishman, J. Effect of thyrotropin on changes in thyroid function following administration of I^{131} to euthyroid cardiac patients. *J. Clin. Endocrinol. & Metabol.*, 1954, *14*, 572–578.

84. Lawson, A., Rimington, C., and Searle, C. E. Antithyroid activity of 2-carbethoxythio-1-methylglyoxaline. *Lancet*, 1951, *2*, 619–621.

85. Lerman, J. Physiologic activity of l-triiodothyronine. *Tr. Am. Goiter A.*, 1953, 10–18.

86. Lerman, J., Jones, H. W., and Calkins, E. Studies of two sporadic cretinous brothers with goiter, together with some remarks on relation of hyperplasia to neoplasia. *Ann. Int. Med.*, 1946, *25*, 677–701.

87. Levi, J. E., and Silberstein, H. E. Lack of effect of fluorine ingestion on uptake of iodine^{131} by thyroid gland. *J. Lab. & Clin. Med.*, 1955, *45*, 348–351.

88. Levy, R. P., Kelly, L. W., Jr., Cooper, G. W., and Jefferies, McK. Relationship between thyrotropin effects upon human thyroid hormone release and iodide uptake. *J. Clin. Endocrinol. & Metabol.*, 1955, *15*, 865–866. (Abstr.)

89. Li, M. C., Rall, J. E., MacLean, J. P., Lipsett, M. B., Ray, B. S., and Pearson, O. H. Thyroid function following hypophysectomy in man. *J. Clin. Endocrinol. & Metabol.*, 1955, *15*, 1228–1238.

90. Librach, I. M. Antithyroid action of P.A.S. Letter to editor. *Lancet*, 1952, *2*, 538.

91. Libby, D. A., and Meites, J. Negative effects of antibiotics on thyroid gland. *Science*, 1954, *120*, 354.

92. Lindsay, S., Dailey, M. E., Friedlander, J., Yee, G., and Soley, M. H. Chronic thyroiditis: Clinical and pathologic study of 354 patients. *J. Clin. Endocrinol.*, 1952, *12*, 1578–1600.

93. Lindsay, S., Dailey, M. E., and Jones, M. D. Histologic effects of various types of ionizing radiation on normal and hyperplastic human thyroid glands. *J. Clin. Endocrinol. & Metabol.*, 1954, *14*, 1179–1218.

94. Linsk, J. A., Paton, B. C., Persky, M., Isaacs, M., and Kupperman, H. S. Effect of phenylbutazone and related analogue (G25671) upon thyroid function. *J. Clin. Endocrinol. & Metabol.*, 1957, *17*, 416–423.

95. MacGregor, A. G., and Somner, A. R. Antithyroid action of para-aminosalicylic acid. *Lancet*, 1954, *2*, 931–936.

96. Macgregor, A. G., and Miller, H. Antithyroid activity of 2-carbithoxythio-1-methylglyoxaline. *Lancet*, 1953, *1*, 881–882.

97. Macks, R. E. Use of radioactive iodine in diagnosis and treatment of hyperthyroidism. *J. Missouri M. A.*, 1953, *50*, 267-271. (Abstr. *Radiology*, 1958, *62*, 313.)

98. Maloof, F., Vickery, A. L., and Rapp, B. Evaluation of various factors influencing treatment of metastatic thyroid carcinoma with I^{131}. *J. Clin. Endocrinol. & Metabol.*, 1956, *16*, 1–27.

99. McConahey, W. M., Owen, C. A., Jr., and Keating, F. R., Jr. Clinical appraisal of radioiodine tests of thyroid function. *J. Clin. Endocrinol. & Metabol.*, 1956, *16*, 724–734.

100. McConahey, W. M., and Owen, C. A., Jr. Studies of inhibitory effect of l-triiodothyronine on thyroidal I^{131} uptake in euthyroid persons and patients with exophthalmic goiter. *J. Clin. Endocrinol. & Metabol.*, 1956, *16*, 1480–1486.

101. McConahey, W. M., and Keating, F. R., Jr. Radioiodine studies in thyroiditis. *J. Clin. Endocrinol.*, 1951, *11*, 1116–1122.

102. McDermott, W. V., Jr., Morgan, W. S., Hamlin, E., Jr., and Cope, O. Cancer of thyroid. *J. Clin. Endocrinol. & Metabol.*, 1954, *14*, 1336–1354.

103. McGirr, E. M., and Hutchison, J. H. Studies in non-endemic goitrous cretinism. *Lancet*, 1953, *1*, 1117–1120.

104. Menge, H., and Conner, M. H. Effect of chlortetracycline on chick thyroid size. *Proc. Soc. Exper. Biol. & Med.*, 1955, *88*, 216–218.

105. Meyers, J. H., and Man, E. B. Artifactual values of serum precipitable iodine after clinical intramuscular injections of mercuhydrin. *J. Lab. & Clin. Med.*, 1951, *37*, 867–869.

106. Mitchell, M. L., Burrows, B. A., Dell, E. S., and Graham, D. E. Effect of thyroid-stimulating hormone on thyroidal iodine turnover. *J. Clin. Endocrinol. & Metabol.*, 1956, *16*, 979–980. (Abstr.)

107. Morgans, M. E., and Trotter, W. R. Antithyroid effect of phenylbutazone. *Lancet*, 1955, *2*, 164–165.

108. MORGANS, M. E., Oldham, A. K., and TROTTER, W. R. Effect of exogenous thyroxine on radioiodine uptake in normal subjects and in cases of thyrotoxicosis in remission. *J. Endocrinol.*, 1952, *8*, 250–253.

109. MUELLER, R., BRAUSCH, C. C., HIRSCH, E. Z., BENUA, R. S., and DOBYNS, B. W. Uptake of radioactive iodine in thyroid of patients with impaired liver function. *J. Clin. Endocrinol. & Metabol.*, 1954, 14, 1287–1299.

110. NACHIMSON, H. I., BENSON, R. H., SZAFIR, J. J., TURNER, R. B., ALLEN, H. C., JR., and TALMAGE, R. V. Comparative study of effects of phenothiazine and iodine on thyroid uptake of I^{131}. *Proc. Soc. Exper. Biol. & Med.*, 1954, *87*, 157–162.

111. NEWMAN, S., and CUPP, C. M. Influence of iodoalphionic acid (priodax), with and without thyrotropin on thyroidal I^{131} uptake in euthyroid patients. *J. Clin. Endocrinol. & Metabol.*, 1957, *17*, 84–98.

112. NOBLE, M. J. D., and ROWLANDS, S. Utilization of radio-iodine during pregnancy. *J. Obst. & Gynaec., Brit. Emp.*, 1953, *60*, 892–894.

113. OLINER, L., KOHLENBRENER, R. M., FIELDS, T., and KUNSTADTER, R. H. Thyroid function studies in children. *J. Clin. Endocrinol. & Metabol.*, 1957, *17*, 61–75.

114. PAPPER, S., BURROWS, B. A., INGBAR, S. H., SISSON, J. H., and ROSS, J. F. Effects of L-thyroxine sodium on non-toxic goiter, on myxedema, and on thyroid uptake of radioactive iodine. *New England J. Med.*, 1952, *247*, 897–899.

115. PASCHKIS, K. E., CANTAROW, A., and PEACOCK, W. C. Influence of estrogens on thyroid function as measured by uptake of radio-active iodine. *Proc. Soc. Exper. Biol. & Med.*, 1948, *68*, 485–486.

116. PERLMUTTER, M., WEISENFELD, S., SLATER, S., and WALLACE, E. Z. Study of inhibition of thyroid gland induced by ingestion of thyroid substance. *J. Clin. Endocrinol. & Metabol.*, 1952, *12*, 208–227.

117. PERLMUTTER, M., and RIGGS, D. S. Thyroid collection of radioactive iodide and serum protein-bound iodine concentration in senescence in hypothyroidism and in hypopituitarism. *J. Clin. Endocrinol.*, 1949, *9*, 430–439.

118. PERLOFF, W. H. Thyrotoxicosis following acute thyroiditis: Report of 5 cases. *J. Clin. Endocrinol. & Metabol.*, 1956, *16*, 542–546.

119. PERLOFF, W. H., LEVY, L. M., and DESPOPOULOS, A. Use of thyrotropic hormone (TSH) in diagnosis of myxedema. *J. Clin. Endocrinol.*, 1951, *11*, 1495–1502.

120. PERRY, W. F., and HUGHES, J. F. S. Urinary excretion and thyroid uptake of iodine in renal disease. *J. Clin. Invest.*, 1952, *31*, 457–463.

121. PITT-RIVERS, R., HUBBLE, D., and HOATHER, W. H. Chromatographic study of thyroidal iodine metabolism in non-toxic nodular goiter. *J. Clin. Endocrinol. & Metabol.*, 1957, *17*, 1313–1323.

122. POCHIN, E. E. Investigation of thyroid function and disease with radioactive iodine. *Lancet*, 1950, *2*, 84–91.

123. POCHIN, E. E. Iodine uptake of human thyroid throughout menstrual cycle and in pregnancy. *Clin. Sc.*, 1952, *11*, 441–445.

124. POCHIN, E. E. Investigation of thyroid function and disease with radioactive iodine. *Lancet*, 1950, *2*, 41–46.

125. QUERIDO, A., and STANBURY, J. B. Response of thyroid gland to thyrotropic hormone as aid in differential diagnosis of primary and secondary hypothyroidism. *J. Clin. Endocrinol.*, 1950, *10*, 1192–1201.

126. RECANT, L., and RIGGS, D. S. Thyroid function in nephrosis. *J. Clin. Invest.*, 1952, *31*, 789–797.

127. REINECKE, E. P., and SOLIMAN, F. A. Cyclic variations in thyroid function of female rats. *Fed. Proc.*, 1953, *12*, 114.

128. ROCHE, M., and LAYRISSE, M. Effect of cobalt on thyroidal uptake of I^{131}. Letter to editor. *J. Clin. Endocrinol. & Metabol.*, 1956, *16*, 831–833.

129. ROGERS, W. R., and ROBBINS, L. R. Iodipamide (cholografin) administration: Its effect on thyroid uptake of I^{131} and serum precipitable iodine in euthyroid persons. *New England J. Med.*, 1955, *253*, 424–425.

130. ROSENBERG, I. N. Antithyroid activity of some compounds that inhibit peroxidase. *Science*, 1952, *116*, 503–505.

131. RUPP, J. J., and PASCHKIS, K. E. Co-existence of Addison's disease and thyrotoxicosis. *J. Clin. Endocrinol. & Metabol.*, 1957, *17*, 143–147.

132. SELENKOW, H. A., RIVERA, A., and THORN, G. W. Effect of amphenone on thyroid function in man. *J. Clin. Endocrinol. & Metabol.*, 1957, *17*, 1131–1140.

133. SCAZZIGA, B. R., BARBIERI, L. L., and BERAUD, T. La fonction thyroïdienne dans les affections du parenchyme hépatique. *Schweiz. med. Wchnschr.*, 1955, *85*, 471–477.

134. SCHNEEBERG, N. G., PERLOFF, W. H., and LEVY, L. M. Diagnosis of equivocal hypothyroidism using thyrotropic hormone (TSH). *J. Clin. Endocrinol. & Metabol.*, 1954, *14*, 223–231.

135. SCHULTZ, A. L., FLINK, E. B., KENNEDY, B. J., and ZIEVE, L., Exchangeable character of accumulated I^{131} in thyroid gland of goitrous

cretin. *J. Clin. Endocrinol. & Metabol.*, 1957, *17*, 441–444.

136. Schultz, A. L., and Jacobson, W. E. Effect of propylthiouracil on thyroid uptake of I^{131} and plasma conversion ratio in hyperthyroidism. *J. Clin. Endocrinol. & Metabol.*, 1952, *12*, 1205–1214.

137. Scott, K. O., Frerichs, J. B., and Reilly, W. A. Effect of Butazoidine® upon fate of I^{131} in rat. *Proc. Soc. Exper. Biol. & Med.*, 1953, *82*, 150–152.

138. Sharrer, N. E., and Asper, S. P., Jr. Inhibition of thyroidal radioiodine uptake following intravenous administration of thyroxine to normal and to hypophysectomized adult subjects. *J. Clin. Endocrinol. & Metabol.*, 1956, *16*, 1311–1325.

139. Shellabarger, C. J. Effect of n-methyl-phenyl-ethyl-barbituric acid on thyroid function in rat. *Endocrinology*, 1956, *58*, 347–351.

140. Shellabarger, C. J., and Schatzlein, F. C. Antithyroid properties of 2-amino,5-nitrothiazole in rats. *Proc. Soc. Exper. Biol. & Med.*, 1955, *90*, 470–473.

141. Sherer, M. G., and Siefring, B. N. Effect of prednisone and prednisolone on thyroid function, with special reference to thyroxine-binding protein in nephrosis. *J. Clin. Endocrinol. & Metabol.*, 1956, *16*, 643–652.

142. Shipley, R., and Chudzik, E. B. Thyroidal uptake and plasma clearance of I^{131} and I^{127} in cirrhosis of liver. *J. Clin. Endocrinol. & Metabol.*, 1957, *17*, 1229–1236.

143. Shipley, R. A., and MacIntyre, F. H. Effect of stress, TSH and ACTH on level of hormonal I^{131} of serum. *J. Clin. Endocrinol. & Metabol.*, 1954, *14*, 309–317.

144. Skanse, B. Radioactive iodine in diagnosis of thyroid disease. *Acta med. Scandinav.*, 1949, Suppl. 235, *136*, 1–186.

145. Skillern, P. G., Crile, G., Jr., McCullagh, E. P., Hazard, J. B., Lewis, L. A., and Brown, H. Struma lymphomatosa: primary thyroid failure with compensatory thyroid enlargement. *J. Clin. Endocrinol. & Metabol.*, 1956, *16*, 35–54.

146. Slingerland, D. W. Effects of organic iodine compound (priodax) on tests of thyroid function. *J. Clin. Endocrinol. & Metabol.*, 1957, *17*, 82–93.

147. Slingerland, D. W. Influence of various factors on uptake of iodine by thyroid gland. *J. Clin. Endocrinol. & Metabol.*, 1955, *15*, 131–141.

148. Sloan, L. W. Of origin characteristics and behavior of thyroid cancer. *J. Clin. Endocrinol. & Metabol.*, 1954, *14*, 1309–1335.

149. Soliman, F. A., and Reinecke, E. F. Influence of estrogen and progesterone on radioactive iodine uptake by rat thyroid. *Am. J. Physiol.*, 1955, *183*, 63–66.

150. Soliman, F. A., and Reinecke, E. P. Changes in uptake of radioactive iodine by thyroid of rat during estrous cycle. *Am. J. Physiol.*, 1954, *178*, 89–90.

151. Spies, S. N. Effect of mercurial diuretic on thyroid uptake and renal clearance of radioiodine. *Proc. Soc. Exper. Biol. & Med.*, 1954, *86*, 469–471.

152. Stanbury, J. B., Ohela, K., and Pitt-Rivers, R. Metabolism of iodine in 2 goitrous cretins compared with that in 2 patients receiving methimazole. *J. Clin. Endocrinol. & Metabol.*, 1955, *15*, 54–72.

153. Stanbury, J. B., Goldsmith, R. R., and Gillis, M. Myotonic dystrophy associated with thyroid disease. Teaching Clinic. *J. Clin. Endocrinol. & Metabol.*, 1954, *14*, 1437–1443.

154. Stanbury, J. B., and Wyngaarden, J. B. Effect of perchlorate on human thyroid gland. *Metabolism*, 1952, *1*, 533–539.

155. Stanbury, J. B. Cretinism with goiter; case report. *J. Clin. Endocrinol. & Metabol.*, 1951, *11*, 740–742.

156. Stanbury, J. B., and Hedge, A. N. Study of family of goitrous cretins. *J. Clin. Endocrinol. & Metab.*, 1950, *10*, 1471–1484.

157. Stanley, M. M., and Astwood, E. B. 1-methyl-2-mercaptoimidazole: Antithyroid compound highly active in man. *Endocrinology*, 1949, *44*, 588–589.

158. Stanley, M. M., and Astwood, E. B. Response of thyroid gland in normal human subjects to administration of thyrotropin, as shown by studies with I^{131}. *Endocrinology*, 1949, *44*, 49–60.

159. Starr, P., Snipes, G., Liebhold-Schueck, R. Biologic effects of triiodothyronine in human subjects. *J. Clin. Endocrinol. & Metabol.*, 1955, *15*, 98–106.

160. Starr, P., and Liebhold-Schueck, R. Effect of oral thyroxine and tri-iodothyronine on radioactive iodine uptake and serum protein-bound iodine in normal human subjects. *Proc. Soc. Exper. Biol. & Med.*, 1953, *83*, 52–54.

161. Talmage, R. V., Nachimson, H., Kraintz, L., and Green, J. A. Effect of phenothiazine, N. F. (green) on uptake of I^{131} by rat thyroid. *Science*, 1953, *118*, 191–192.

162. Torikai, T., and Kumaoka, S. Effect of para-aminosalicylic acid on hyperthyroidism. *Lancet*, 1956, *1*, 84–85.

163. Taylor, S. Calcium as goitrogen. *J. Clin. Endocrinol. & Metabol.*, 1954, *14*, 1412–1422.

164. Wase, A. W., and Foster, W. C. Thiopental and thyroid metabolism. *Proc. Soc. Exper. Biol. & Med.*, 1956, *91*, 89–91.

165. Wase, A. W., and Greenspan, J. Effect of so-

dium 5-allyl-5-(1-methylbutyl) 2-thiobarbiturate on uptake of I^{131} by rat thyroid. *Proc. Soc. Exper. Biol. & Med.*, 1953, *84*, 154–155.

166. WERNER, S. C., BLOCK, R. J., and MANDL, R. H. Circulating iodoproteins in nongoitrous adult with primary amenorrhea, body deformities, and normal levels of serum precipitable iodine and thyroidal I^{131} uptake. *J. Clin. Endocrinol. & Metabol.*, 1957, *17*, 1141–1149.
167. WERNER, S. C., BLOCK, R. J., MANDL, R. H., and KASSENAAR, A. A. H. Pathogenesis of case of congenital goiter with abnormally high levels of SPI and with mono- and diiodotyrosin in serum. *J. Clin. Endocrinol. & Metabol.*, 1957, *17*, 817–831.
168. WERNER, S. C., and HAMILTON, H. Hyperthyroidism without apparent hypermetabolism. *J.A.M.A.*, 1951, *146*, 450–453.
169. WERNER, S. C., QUIMBY, E. H., and SCHMIDT, C. Use of tracer doses of radioactive iodine, I^{131}, in study of normal and disordered thyroid function in man. *J. Clin. Endocrinol.*, 1949, *9*, 342–354.
170. WHITELAW, M. J., THOMAS, S., and REILLY, W. A. Nongoitrous cretin with high level of serum PBI, and thyroidal I^{131} uptake. *J. Clin. Endocrinol. & Metabol.*, 1956, *16*, 983. (Abstr.)
171. WILANSKY, D. L., NEWSHAM, L. G. S., and HOFFMAN, M. M. Influence of senescence on thyroid function; functional changes evaluated with I^{131}. *Endocrinology*, 1957, *61*, 327–336.
172. WILKINS, L., CLAYTON, G. W., and BERTHRONG, N. Development of goiters in cretins without iodine deficiency: Hypothyroidism due to apparent inability of thyroid gland to synthesize hormone. *Pediatrics*, 1954, *13*, 235–246.
173. WITTER, R. F., NEWCOMB, E. H., and STOTZ, E. Studies on mechanism of action of dinitrophenol. *J. Biol. Chem.*, 1953, *202*, 291–303.
174. WOLFF, J., RUBIN, L., and CHAIKOFF, I. L. Influence of 2,4-dinitrophenol on plasma protein-bound iodine. *J. Pharmacol. & Exper. Therap.*, 1950, *98*, 45–48.
175. WONG, T., HOGNESS, J. R., and WILLIAMS, R. H. Effect of p-aminosalicylic acid on thyroid and adrenal. *Proc. Soc. Exper. Biol. & Med.*, 1953, *82*, 598–601.
176. WOOLNER, L. B., MCCONAHEY, W. M., and BEAHRS, O. H. Invasive fibrous thyroiditis (Riedel's struma). *J. Clin. Endocrinol. & Metabol.*, 1957, *17*, 201–220.
177. WOOLNER, L. B., MCCONAHEY, W. M., and BEAHRS, O. H. Granulomatous thyroiditis (de Quervain's thyroiditis). *J. Clin. Endocrinol. & Metabol.*, 1957, *17*, 1202–1221.
178. WYNGAARDEN, J. B., WRIGHT, B. M., and WAYS, P. Effect of certain anions upon accumulation of retention of iodide by thyroid gland. *Endocrinology*, 1952, *50*, 537–549.
179. ZINGG, W., and PERRY, W. F. Influence of adrenal and gonadal steroids on uptake of iodine by thyroid gland. *J. Clin. Endocrinol. & Metabol.*, 1953, *13*, 712–723.

IMPORTANCE OF THE DETERMINATION OF THE WEIGHT OF THE THYROID GLAND AND CLINICAL BIOLOGIC FACTORS IN THE TREATMENT OF HYPERTHYROIDISM WITH I^{131}*

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IT IS the purpose of this paper to review the results in our laboratory of treatment of hyperthyroidism with I^{131} since the introduction of the *pneumothyroid method* for the evaluation of the thyroid weight,[2,4,5] and to correlate the results with the physical, clinical and biologic factors involved.

The patients with hyperthyroidism who were selected for treatment with I^{131} in the twenty to forty year age group consisted of persons who had recurrence after thyroidectomy, who failed to respond to or developed severe symptoms after treatment with antithyroid drugs, who concomitantly with hyperthyroidism had cardiac disease, diabetes or malignant neoplasms, and a few who had refused to undergo operation. Above forty years of age patients with severe hyperthyroidism who had had no former therapy were also treated.

If on the basis of available clinical and laboratory evidence I^{131} therapy is decided upon, a tracer study with carrier free I^{131} is performed in the routine way,[6] usually one to two weeks preliminary to the administration of the therapeutic dose.

From the I^{131} uptake curve as described previously,[4] the following formula is used to calculate the dose administered, A (in millicuries), in order to deliver an absorbed dose, D (in rad), to the thyroid gland of weight M (in grams):

$$A = \frac{MD}{1.05 \int_0^{t_n} p \cdot dt + 1.52 p_n T_e} .10^{-4} \text{ mc} \qquad (1)$$

where T_e is the effective half-life of the I^{131} in the gland which we assume to be definitely defined t_n days after the administration of the radionuclide and p_n is the fraction of the activity remaining in the thyroid gland t_n days after.

A graphic integration gives the integral value

$$\int_0^{t_n} p \cdot dt = \sum_1^n p_i (i = 1, 2, \cdots, n) \qquad (2)$$

where p_i is the average of the fraction of the administered radioactivity existing in the gland during the i^{th} day.

Of course, this is an average dose, assuming a uniform distribution in the gland, a 10 per cent contribution from the gamma radiation and an average beta energy of 0.187 mev.

After the administration of the dose A, the I^{131} uptake curve is determined in order to calculate the absorbed dose *effectively* delivered to the gland.

Aside from unknown biologic principles, the most important factor for accurate dosage is the precise determination of the weight of the thyroid gland. Until re-

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cently, two methods were used for this purpose: (1) The palpation of the gland, which Loevinger termed the "method of calibrated fingers"; and (2) the estimation of the size of the gland by means of collimated scintillation counters[1,3,7] by using empirical formulae to calculate the weight from the area of the frontal projection and the length of the thyroid gland. The suggestion to determine its thickness from the gradient of the isocount curves was also made.

PNEUMOTHYROID

For the past few years our laboratory has devoted special attention to this important problem.[2,4,5]

Since the thyroid gland capsule is surrounded by loose areolar tissue, the injection of gas permits contrast roentgen visualization, which accurately delineates its borders and dimensions. The method is similar to retropneumoperitoneum and is called "pneumothyroid."

The technique is as follows: The patient is placed on his left side to reduce the possibility of gas embolism. After novocain infiltration of the skin in the midline of the infrahyoid region, a 0.7 mm. caliber needle is introduced and advanced until the middle cervical fascia is pierced. At this point the patient is asked to swallow several times, the up and down movement of the needle ensuring that it is in the right place. Oxygen is used as contrast material and the injection is carried out by using an apparatus similar to that employed in pneumothorax. Attached to the needle is a rubber tube, to which is connected a syringe (an aspiration is done first to rule out possible injection of a blood vessel) and a manometer to measure the pressure of injection, which must be kept as low as possible (usually 2–3 cm. Hg). The amount of injected oxygen varies from case to case but is about 300 cc. on an average. After the injection is completed, roentgenograms and laminagrams are made in two perpendicular projections.

The method is not dangerous and has already been used successfully in 150 cases without any ill effects.

FIG. 1. Pneumothyroid laminagram showing an intrathoracic goiter.

The volume of the thyroid is determined from the roentgenographic or laminagraphic image by comparing each lobe to a scalene ellipsoid with semi-axes a,b,c that can be measured directly and by correcting for the magnification due to distance when necessary.

The volume is given by

$$V = \frac{4}{3}\pi abc.$$

This is a simplifying approximation of the problem since commonly the thyroid gland presents very variable and irregular outlines and shapes. Figure 1 illustrates a pneumothyroid which is particularly interesting since it serves to visualize an intrathoracic goiter, permitting the clarification of certain diagnostic problems and the determination of the exact therapeutic dose of I^{131}. Figure 2 shows a scintigram of the same case. Figure 3,*A* and *B* demonstrates the value of pneumothyroid in establishing the response to treatment. According to the calculations, the weight of the thyroid

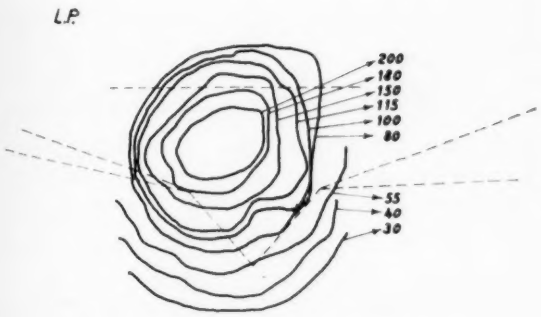

Fig. 2. Scintigram corresponding to the intrathoracic goiter of Figure 1.

gland has been reduced from the original 80 gm. to 30 gm. seven months after the administration of I^{131}.

It is possible to calculate more accurately the weight of the thyroid gland by using models made from the roentgenograms or laminagrams as we have tried in a few cases but the procedure is time consuming. In this respect, the projection in the normal axis is considerably more helpful, since in the lateral view not infrequently there is an overlapping of the two lobes.

A comparative study of the results of different investigators is of considerable aid in estimating the relative merit of the various methods used for the determination of the weight of the thyroid gland, such as the empirical relationship between the weight of the gland and the projected area and length obtained from necropsy, surgical specimens, scintigraphy and now pneumothyroid.[2]

Figure 4 shows the contours of the gland obtained with the pneumothyroid method in 44 cases.

Allen and Goodwin[1] assuming a relationship between the volume V, the projected area S and the length L expressed by the formula

$$V = kSL \qquad (3)$$

obtained $k=0.32$ from scintigrams in 10 cases.

Himanka and Larsson[8] assuming two relationships, the empirical formula (3) and the formula on the top of next page.

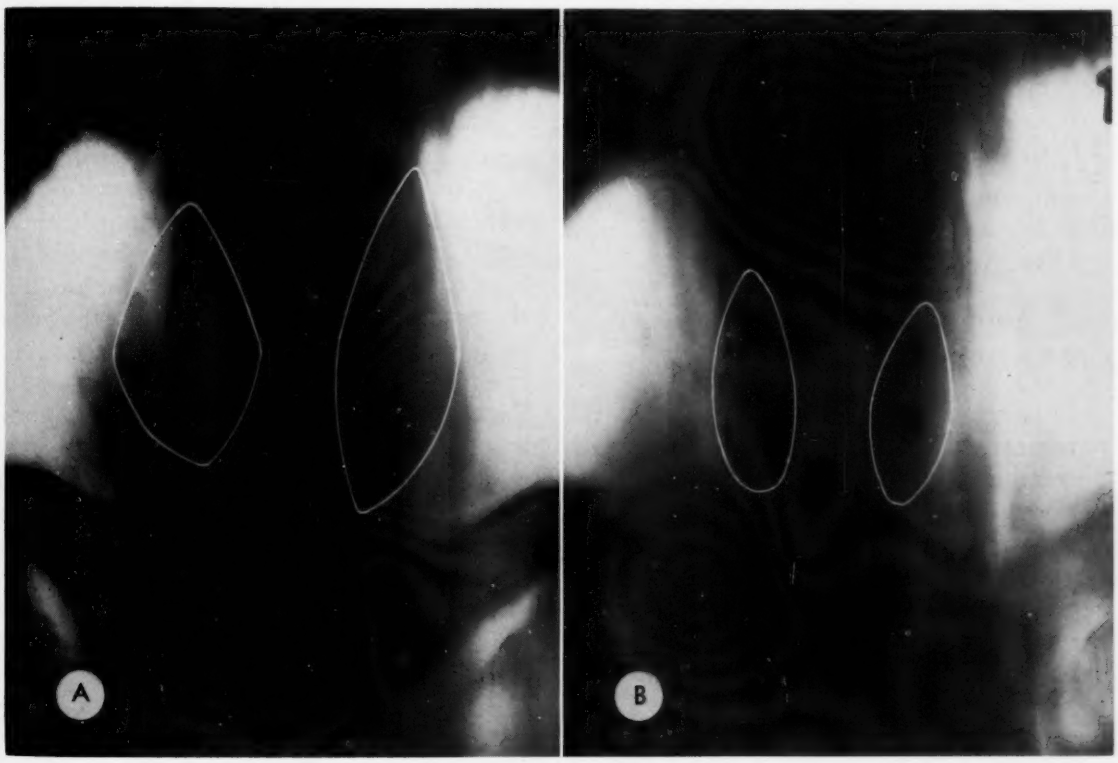

Fig. 3. Pneumothyroid laminagrams showing reduction in the volume of the gland after treatment with I^{131}. The gland weighed 83 gm. before (*A*) and 30 gm. after (*B*) treatment.

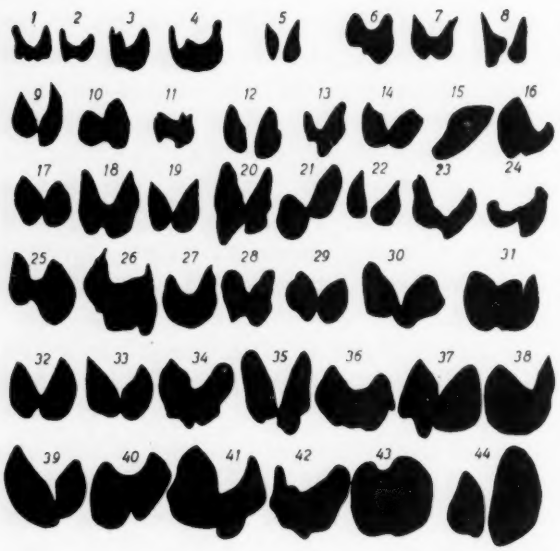

FIG. 4. Thyroid gland contours obtained from pneumothyroid laminagrams. (Baptista and Franco.[2])

$$V = K(\sqrt{S})^3, \qquad (4)$$

obtained from thyroid glands removed at necropsy in a study of 44 cases the values

$$K = 0.27 \pm 0.06$$

$$K = 0.33 \pm 0.06.$$

In our own study[2] adjusting the numerical values to the following equations

$$V = kSL + v_1 \qquad (5)$$

and

$$V = k(\sqrt{S})^3 + v_2 \qquad (6)$$

we obtain the values

$$k = 0.31 \pm 0.05 \qquad v_1 = 5.8 \text{ cm.}^3$$

$$k = 0.37 \pm 0.04 \qquad v_2 = 7.4 \text{ cm.}^3$$

It is remarkable that the values of the parameters should show such an agreement. Nevertheless, the deviations are sufficiently important in all studies to render the use of an empirical formula rather inaccurate. For instance, Kelly[9] from scintigrams in 15 cases found a maximum deviation of 150 per cent with an average of 49 per cent using $k=0.32$. We obtained deviations of 107 per cent with an average of 25 per cent for equation (5) and about 60 per cent and 24 per cent for equation (6). Needless to say, the collimation of the detector changes the empirical parameter of the relationships.

MATERIAL AND RESULTS OF I^{131} THERAPY

From September, 1952 to September, 1957, 140 patients with hyperthyroidism were treated with I^{131} therapy. Of these, 117 were followed-up and form the subject of the present study.

The sex incidence was 7 men (6 per cent) to 110 women (94 per cent). The ages of the patients ranged from twenty-five years to eighty years, with the majority in the fourth and fifth decades of life. The time between the onset of the illness and the treatment varied from one to twenty-nine years; however, the greatest number had a history of hyperthyroidism of less than five years' duration.

Clinically, the hyperthyroidism was divided into: grave, 52 patients (44 per cent); moderate, 56 patients (47 per cent); and mild, 9 patients (7 per cent). Seventeen patients had the following complications: heart disease, 9; diabetes, 6; vitiligo, 1; and malignant exophthalmos, 1. Exophthalmos was present in 45 patients; in 1 it was very severe, in 2 it was severe, in 29 it was moderate and in 13 it was slight.

The type of goiter was diffuse in 74 patients, nodular in 14 patients, multinodular in 3 patients and 26 patients had no enlargement of the thyroid gland.

All patients were treated with I^{131} according to the scheme already described. In the beginning, the prescribed absorbed dose varied according to the clinical case, averaging 9,600 rad (12,000 rep). However, as low dosage appeared more useful, this was later reduced to 8,300 rad (10,000 rep). The majority of patients received doses between 5,000 and 14,000 rad. The single administered dose varied from 1.5 mc to about 40 mc I^{131}.

The bars in Figure 5 indicate the percentage deviations of the administered doses relative to the prescribed absorbed dose calculated from the formula

$$\frac{D_a - D_p}{D_p} \times 100$$

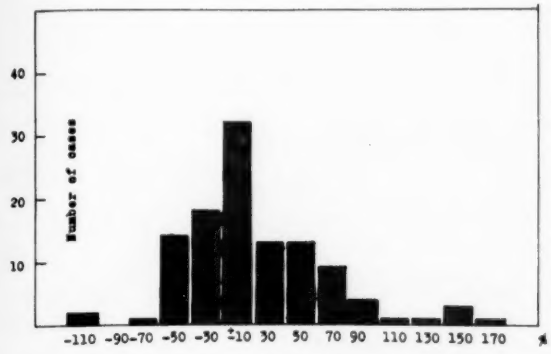

Fig. 5. Percentage deviations, $(D_a/D_p - 1)$ 100 per cent, of the administered doses D_a relative to the prescribed absorbed dose D_p.

in which D_a is the administered dose and D_p the prescribed absorbed dose. It may be noted that the most frequent deviation was around 10 per cent, although in a great number of cases it reached 30 per cent.

In a similar manner the bars in Figure 6 indicate the percentage deviations of the effective half-life before treatment and during treatment calculated from the formula

$$\frac{T_{th} - T_{pth}}{T_{pth}} \times 100$$

in which T_{th} is the effective half-life during treatment and T_{pth} the effective half-life before treatment. The greatest deviation in a large number of cases was likewise around 30 per cent.

The differences between the prescribed absorbed dose and the administered dose

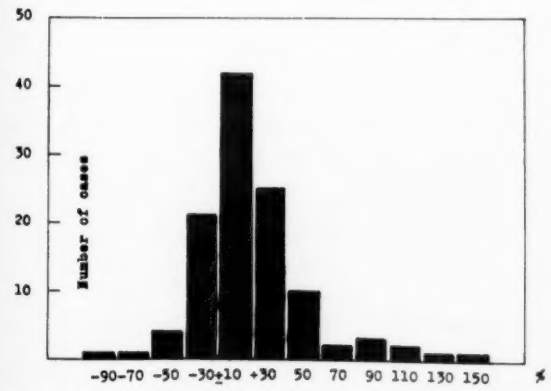

Fig. 6. Percentage deviations, $(T_{th}/T_{pth} - 1)$ 100 per cent, of the effective half-life before treatment T_{pth} and during treatment T_{th}.

are due to variations of the I^{131} thyroid uptake curve with the tracer and the therapeutic radioactivities. It is difficult to find a reasonable explanation for this discrepancy.

The interval between the pretherapeutic I^{131} test and the treatment is, with a few exceptions, less than two weeks so as to avoid a variation of the behavior of the gland.

For the same reason, every procedure that interferes with the iodine metabolism is suspended for at least one month prior to I^{131} therapy. Despite this, some glands with an unsteady behavior may account for the differences of the received doses. In our series, there was no relationship between the effective half-life and the uptake variation of the I^{131} and the age of the patient, the duration of the disease, the severity of the hyperthyroidism and the physical characteristics, including the weight, of the thyroid gland.

Although in principle we may assume an influence of the therapeutic dose on the I^{131} uptake curve, the data available failed to substantiate any such correlation.

The results obtained were classified into four groups: (1) remission; (2) improvement; (3) recurrence; and (4) hypothyroidism. The criteria of selection were based on the clinical and laboratory data, including the I^{131} test. Each group was divided into two subgroups, according to whether the thyroid mass was determined by pneumothyroid or by palpation. Only the cases which received a single therapeutic dose are considered here. The recurrences will be discussed later. The percentages of the results are portrayed graphically in Figure 7. As may be seen, pneumothyroid was performed on 77 patients and the mass of the thyroid was determined by palpation in 40 patients. The percentage of remissions was higher (70 per cent) in the patients with pneumothyroid than in those in whom palpation was used (45 per cent). Conversely, the percentages of improvement (8 per cent), recurrence (17 per cent) and hypothyroidism (5 per cent) were lower than in the corresponding groups with palpation, where the figures were 15, 27.5 and

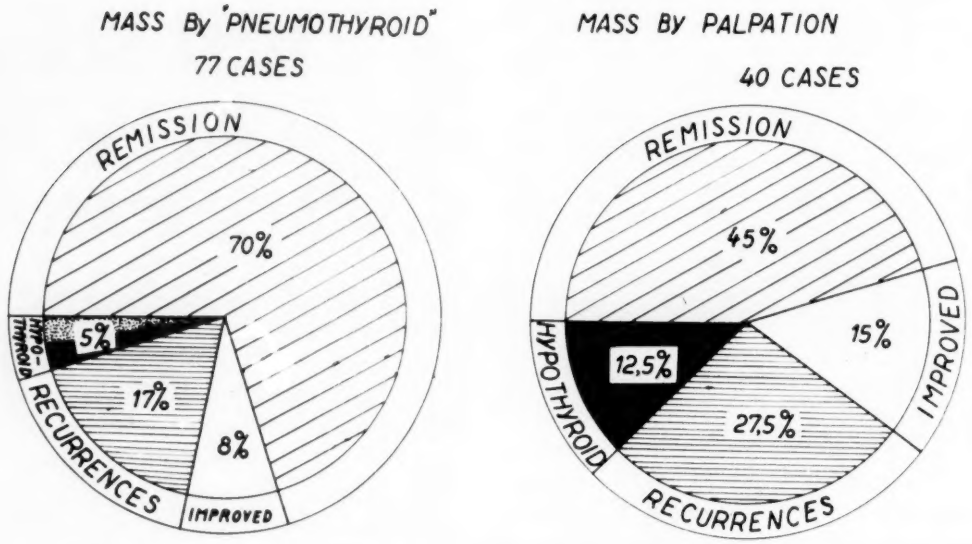

FIG. 7. Graphs summarizing the results of treatment of hyperthyroidism with I^{131} in two groups of patients in whom the thyroid weight was estimated by pneumothyroid and by palpation.

12.5 per cent, respectively. The relatively lower percentage of hypothyroidism is particularly gratifying. If the 2 patients who at the time of pneumothyroid were classified as slightly hypothyroid are omitted, the percentage of I^{131} induced hypothyroidism falls to 2.5 per cent in this group. In 2 other patients with remissions who developed slight hypothyroidism, the thyroid function returned to normal within two to three years after therapy.

The absorbed dose in the successfully treated patients who had undergone pneumothyroid varied between 4,400 and 20,000 rad with 8,000 to 9,000 rad in most instances (Fig. 8).

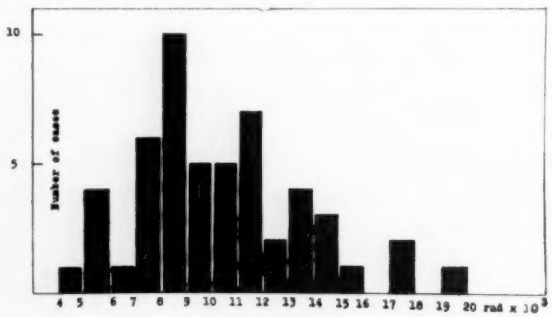

FIG. 8. Absorbed dose in rad effectively delivered in patients in whom remission was obtained after treatment with I^{131} and whose thyroid weight was estimated by pneumothyroid.

The number of patients in the improved, recurrent and hypothyroid groups is too small to permit proper statistical analysis. Tables I, II and III list individually the cases treated and the dosage received. It may be noted that of 9 hypothyroid patients 6 received higher doses than 10,450 rad (Table III) and of 24 patients with recurrence, 11 received lower doses than 7,000 rad (Table II). One of the patients who received 174 rad had an accidental

TABLE I

IMPROVED CASES

Case No.	Dose (rad)	Thyroid Mass Determined by	
		Pneumothyroid	Palpation
99374	4,810	+	
109460	5,310	+	
145320	6,220		+
106305	6,630	+	
112541	7,820		+
144427	8,660	+	
123330	9,540	+	
125350	10,000		+
112706	10,900		+
131530	12,500	+	
104442	13,950		+
136648	14,800		+

TABLE II

RECURRENCES

Case No.	Dose (rad)	Thyroid Mass Determined by	
		Pneumothyroid	Palpation
130715	174	+	
121859	628		+
92602	946		+
98116	1,985		+
102943	5,730	+	
93599	5,770		+
100816	6,000	+	
100831	6,200		+
129637	6,230	+	
90492	6,700	+	
137882	6,750		+
110154	7,670	+	
136722	7,740		+
144180	7,800	+	
115745	8,000		+
100889	8,540		+
116138	9,660		+
108285	10,000	+	
92403	12,450	+	
40129	13,350	+	
103075	13,850	+	
131433	17,750	+	
130856	30,500	+	
100468	—		+

saturation of the thyroid. It is difficult to explain how a patient who received 30,500 rad sustained recurrence and how a patient who received 4,350 rad developed hypothyroidism (both patients had pneumothyroid).

TABLE III

HYPOTHYROIDISM

Case No.	Dose (rad)	Thyroid Mass Determined by	
		Pneumothyroid	Palpation
146765	4,350	+	
145492	6,560		+
150139	7,090		+
115096	10,450	+	
97336	10,650		+
117190	12,500		+
139641	12,600		+
123457	13,700	+	
129675	15,650	+	

TABLE IV

RECURRENCES SUCCESSFULLY TREATED BY A SECOND DOSE OF I^{131} (PNEUMOTHYROID GROUP)

First Treatment		Second Treatment	
Weight (gm.)	Dose (rad)	Weight (gm.)	Dose (rad)
120	6,700	30	9,300
70	6,230	30	6,300
83	30,500	30	13,100

In the recurrent group of 24 patients, 3 failed to submit to further treatment. In 3 cases of the penumothyroid subgroup, a good result was obtained following a second dose of therapeutic I^{131} (Table IV). Pneumothyroid after the second treatment revealed reduction in the weight of the thyroid gland in all. Five patients received I^{131} therapy three times. Of these, 1 responded satisfactorily, 1 developed hypothyrodism, 1 had some remission and the other 2 did not return for follow-up. Of 13 patients in whom the weight of the thyroid gland was determined by palpation, 6 had remissions following repeated treatment, 3 developed hypothyroidism and 4 did not return for follow-up.

Study of the causes of therapeutic failure revealed no influence of the age of the patient or the duration of the disease, the statistical distribution being similar in regard to both of these factors. The effect of the type of goiter and of the severity of disease on the radiation response is analyzed in Table V. As may be seen, the most favorable results in all types and degrees were obtained when the weight of the thyroid gland was determined by the pneumothyroid method.

SUMMARY AND CONCLUSIONS

Analysis of the results and an independent assay by the Endocrinology Service of the 117 hyperthyroid patients treated with I^{131}, in 77 of whom the weight of the

TABLE V

RESULTS BASED ON TYPE OF LESION AND SEVERITY OF DISEASE

Type of Lesion and Severity of Disease	Remission				Improvement				Recurrence				Hypothyroidism				Total Cases	
	Pneumothyroid		Palpation		Pneumothyroid		Palpation		Pneumothyroid		Palpation		Pneumothyroid		Palpation		Pneumothyroid	Palpation
	Cases	Per Cent	Cases	Per Cent	Cases	Per Cent	Cases	Per Cent	Cases	Per Cent	Cases	Per Cent	Cases	Per Cent	Cases	Per Cent		
Diffuse Goiter	29	60	13	50	5	10	4	15	10	21	6	23	4	8	3	12	48	26
Nodular Goiter	8	89	1	13	—	—	2	25	1	11	5	63	—	—	—	—	9	8
Without Goiter	16	84	5	71	1	5	—	—	2	10	—	—	—	—	2	29	19	7
Grave Hyperthyroidism	19	60	6	30	3	10	1	5	9	28	10	50	1	5	3	10	32	20
Moderate Hyperthyroidism	33	79	8	57	2	5	5	35	4	9	—	—	3	7	1	7	42	14
Mild Hyperthyroidism	3	—	3	—	1	—	—	—	—	—	1	—	—	—	1	—	4	5

thyroid gland was determined by pneumothyroid which originated in our laboratory in 1953 and in 40 by estimation from palpation, permit the following conclusions:

1. In the pneumothyroid group remissions after a single dose were obtained in 70 per cent of the cases as against 54 per cent in the other group.

2. In the pneumothyroid group improvement was noted in 8 per cent of the cases as against 15 per cent in the other group.

3. In the pneumothyroid group recurrences occurred in 17 per cent of the cases as against 27.5 per cent in the other group.

4. In the pneumothyroid group postherapeutic hypothyroidism was observed in only 5 per cent of the cases (2.5 per cent mild cases) as against 12.5 per cent in the other group.

5. No correlation was found between the results and the clinical and biologic factors such as age of the patient, duration and degree of severity of the disease, gland characteristics and type of goiter.

It may, therefore, be stated that determination of the weight of the thyroid gland by the pneumothyroid method enables a more accurate dosage in the therapeutic application of I^{131} for hyperthyroidism, yielding better clinical results. However, the discrepancy between the prescribed absorbed dose and the administered dose is too important to be ignored and deserves further study.

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REFERENCES

1. Allen, H. C., Jr., and Goodwin, W. E. Scintillation counter as instrument for in vivo determination of thyroid weight. *Radiology*, 1952, *58*, 68–79.
2. Baptista, A. M., and Franco, V. H. Relação entre a projecção frontal da glândula tiroideia e o seu volume. *Rev. ibér. endocrinol.*, 1957, *4*, 441–449.
3. Bauer, F. K., Goodwin, W. E., Libby, R. L., and Claussen, B. Visual delineation of thyroid glands in vivo. *J. Lab. & Clin. Med.*, 1952, *39*, 153–158.
4. Franco, V. H., Quina, M. G., Botelho, L., Palacios, J., Baptista, A. M., Perez-Fernandez, M. A., and Martins, M. L. *Proc. Internat. Conf. Peaceful Uses of Atomic Energy*, Geneva, 1955, 10.
5. Franco, V. H., and Quina, M. G. Pneumo-thyroid; new procedure for determining mass of thyroid gland for radioiodine treatment of hyperthyroidism. *Brit. J. Radiol.*, 1956, *29*, 434–439.
6. Franco, V. H., Botelho, L., Clode, W., Baptista, A. M., Perez-Fernandez, M. A., and Martins, M. L. *Proc. Internat. Conf. Peaceful Uses of Atomic Energy*, Geneva., 1955, 10.
7. Goodwin, W. E., Cassen, B., and Bauer, F. K. Thyroid gland weight determination from thyroid scintigrams with postmortem verification. *Radiology*, 1953, *61*, 88–92.
8. Himanka, E., and Larsson, L. G. Estimation of thyroid volume; anatomic study of correlation between frontal silhouette and volume of gland. *Acta radiol.*, 1955, 43, 125–131.
9. Kelly, F. J. Observations on calculation of thyroid weight, using empirical formulae. *J. Clin. Endocrinol.*, 1954, 14, 326–335.

THYROID FUNCTION ASSAY WITH RADIOIODINE: THE CORRELATION OF THYROIDAL CLEARANCE FACTOR AND PERCENTAGE UPTAKE

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IN PREVIOUS communications our method for determination of thyroidal clearance rate has been described in detail.[1,2,3] Mathematic equations and numerical data were presented describing the early movement of a test dose of radioiodine in the human body. Thyroidal uptake and renal excretion rate factors (or clearance rates) from observed values of the fractions of the net dose in the neck, N, and urine, E, without the need for any blood samples were described. Suitable charts relating N and E to the thyroidal and renal clearance rate factors k_1 and k_2 were presented.

K minutes^{-1} equals the average combined (thyroid plus kidneys) fractional rate of removal of radioiodine from the iodide space during the time interval t, that is, the average fraction of the circulating iodide pool that is removed each minute.

k_1 minutes^{-1} equals the average fractional rate of uptake by the thyroid during time t; k_2 minutes^{-1} equals the average fractional rate of renal excretion during time t.

N equals the fraction of the original dose observed in the neck by external counting at time t including both thyroid and extrathyroid tissues.

t minutes equals the time from injection of the test dose.

In a further presentation it was our purpose to apply the above data to the conversion of several of the diagnostic parameters which are currently in use in this type of investigation so as to achieve a common basis for comparison and to describe our clinical results. A set of diagnostic limits for routine use based on a maximum of published information was provided.

Based upon this series of data the diagnostic values finally adopted were as follows:

The Parameter for Uptake Rate, 10^{-3} k_1 Minutes^{-1}. For the border zone low to euthyroid this value is 0.23 and euthyroid to high 3.85. These values corresponded with 3.7 ml. per minute on the low side to 63 ml. per minute on the high side for thyroidal plasma clearance rates. This further corresponded with 24 hour percentage uptakes of 8 per cent on the low side and 62 per cent on the high side. Protein-bound iodine values corresponding for 100 cc. were 3.9 μg. per cent on the low side to 8.2 on the high side.

It was our present purpose to interrelate our diagnostic limits with percentage thyroid uptakes at one (N_1) and two hours (N_2) and to relate these values to those obtained when one employs the technique which has been described by the Oak Ridge Institute of Nuclear Studies, Medical Division (ORINS, M. D. Techniques).*

TECHNIQUE

The ORINS Medical Division technique is virtually identical to the techniques we have employed for our clearance rate studies with the exception that two lead filters are interposed between the patient and the scintillation detector. The filter A

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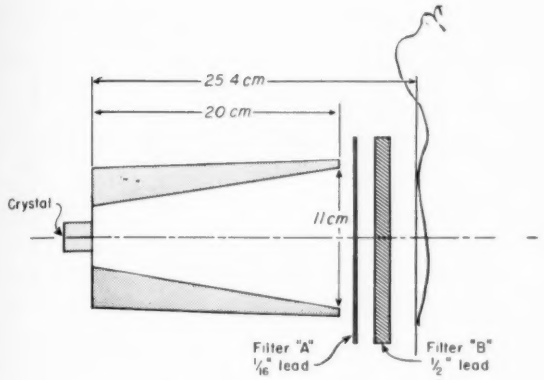

FIG. 1. Schematic diagram of ORINS uptake technique.

measures 1/16 inch in thickness, and the filter B measures ½ inch in thickness. The distance between the scintillation crystal and the patient's neck is 25.4 cm. and a special collimator has been constructed which is virtually identical with the Oak Ridge Medical Division collimator which views an area of the neck which measures 12.7 cm. diameter. This is illustrated diagrammatically in Figure 1.

For uptake observations a collimated scintillation counter is used at a crystal skin distance of 25.4 cm. The lead collimator walls are tapered from a maximum of 3.0 cm. thickness. Its axial aperture has a minimal diameter of 4.5 cm. and it tapers upward with a half angle of 9.2 degrees so that a circle of 20.8 cm. diameter is in full view of the crystal at 50 cm. distance.

In using the ORINS technique we have modified this to the extent that the dose is given intravenously, and we have used a reference solution in a wax phantom rather than a mock iodine standard. To summarize the above, the following counts were made in determining percentage uptake by the ORINS technique:

1. Counts of 4 cc. reference solution (5 min.) (R).
2. Counts of 4 cc. dose solution (5 min.) (d).
3. Counts of residue (5 min.) (*i.e.*, counts remaining in syringe, cotton, etc. after giving dose).
4. Counts over patient's neck for 10 min. with A filter interposed between neck and collimator.
5. Counts over patient's neck for 10 min. with A and B filters interposed between neck and collimator.
6. Counts over the reference solution, R, in a wax phantom with A filter interposed.
7. Counts over the reference solution, R, in a wax phantom with A and B filter interposed.

The exact amount of I^{131} given the patient as compared to the reference (*i.e.*, d/R) can be computed:

$$d/R = \frac{\text{counts of 4 cc. dose solution} - \text{counts of residue}}{\text{counts of 4 cc. reference solution}}$$

The percentage uptake is then obtained by the equation:

$$\%\ \text{uptake} = \frac{\text{patient count with A filter} - \text{patient count with A and B filters}}{(\text{ref. count with A filter} - \text{ref. count with A and B filters}) \times d/R}$$

For the exact technique of neck counting and urine determination in finding thyroidal clearance rate, k_1, the reader is referred to previous publications.[1,2,3] Essentially this consists of determining neck fractions of injected I^{131} at a given time and I^{131} urine excretion to that time. Previously determined corrections for absorption and backscatter in the neck tissues are then applied to the neck and urine results and thyroidal clearance rate obtained through a series of computations. The thyroidal clearance rate obtained is then in essence a measure of thyroidal uptake (corrected for the radiation effect of the neck tissues outside the thyroid) and urinary clearance.

In our study, the percentage uptake at one hour by the ORINS technique and thyroidal clearance rate at one hour were determined on the same patient. A series of such determinations was carried out.

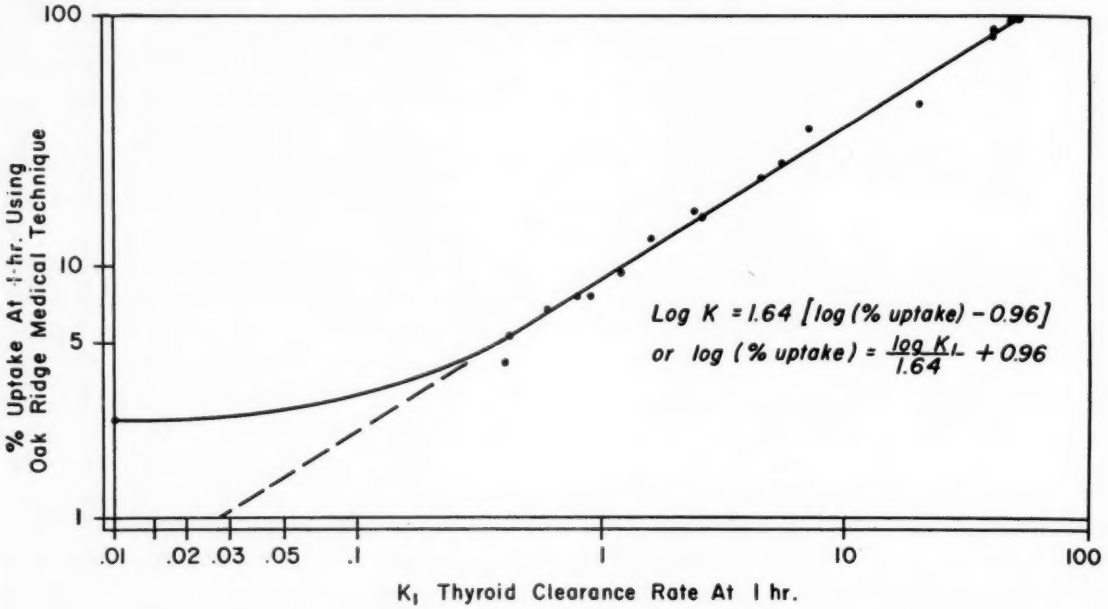
100
10
5
1
% Uptake At ½ hr. Using Oak Ridge Medical Technique
Log K = 1.64 [log (% uptake) - 0.96]
or log (% uptake) = log K1 / 1.64 + 0.96
.01 .02 .03 .05 .1 1 10 100
K1 Thyroid Clearance Rate At 1 hr.

FIG. 2. Log-log relationship of k_1 to first hour percentage uptake by ORINS technique (20 cases).

RESULTS

Relationship of k_1 to First Hour Percentage Uptake by ORINS Technique. The log-log linear relationship between the k_1 factor and the percentage uptake obtained by the ORINS technique in a series of 20 patients is shown in Figure 2. It will be noted that this relationship held true with accuracy in both the high range and relatively low range. In the very low range (k_1 equal 0) this relationship broke down because there is virtually always some reading in relation to percentage uptake because of the neck tissue factor even though the A filter and B filter are applied. Nevertheless, no difficulty in accuracy of relegating a patient to the hypothyroid zone would be obtained.

The log-log linear relationship can be described accurately with the following formula:

$$\log \% \text{ uptake} = 0.610 \log k_1 + 0.96 \quad (1)$$

When one applies this formula to the limits of normal as indicated in Table I, which gives us the diagnostic borderline values which we have finally adopted, one

TABLE I

DIAGNOSTIC BORDERLINE VALUES FINALLY ADOPTED

Parameter	Thyroid Borderline Status			
	Very Low	Low	Euthyroid	High
	Low	Euthyroid	High	Very High
Uptake rate 10^{-3} k_1 minute^{-1}	0.09	0.23	3.85	9.9
Thyroidal plasma clearance rate* ml./min.	1.5	3.7	63	160
24 hour uptake per cent†	3.9	8.0	62‡	82‡
Protein-bound iodine μg. per 100 ml.	2.8	3.9	8.2	10.0
Per cent uptake at one hr.	2.1	3.8	20.8	36

* For V_{30} = 16.3 liter.
† Strictly for the collimator system described (1, 2); these values will not apply for open collimation.
‡ Use of this parameter is not recommended.

TABLE II

COMPARISON OF LIMITS OF NORMAL FOR I^{131} THYROID FUNCTION EVALUATION BY K_1 CLEARANCE RATE FACTOR, ONE AND TWO HOUR PERCENTAGE UPTAKES (INTRAVENOUS TRACER) AND ONE HOUR PERCENTAGE UPTAKE BY ORINS TECHNIQUE, BUT USING INTRAVENOUS TRACER DOSE

Range	$k_1 \times 10^{-3}$	Our Adaptation ORINS Technique Per Cent Uptake at One Hour	N_1 (%)	N_2 (%)
Hypothyroid	<0.18	<3.2	<3.15	4.75
Borderline hypothyroid	0.18 to 0.23	3.2 to 3.8	3.15 to 3.7	4.75 to 5.5
Euthyroid	0.23 to 3.85	3.8 to 20.8	3.7 to 22.5	5.5 to 29.6
Hyperthyroid	above 3.85	above 20.8	above 22.5	above 29.6

finds that the percentage uptake in one hour employing our modified ORINS technique related to the previous clearance rate technique is indicated in the enclosed result. The euthyroid percentage uptake at one hour is noted to be 3.8 to 20.8 per cent (see Table II).

Relationship of k_1 to First and Second Hour Percentage Uptake by Our Technique. In an analysis of 276 consecutive cases, it is apparent that the log-log relationship of the neck fractions, N_1, at the end of the

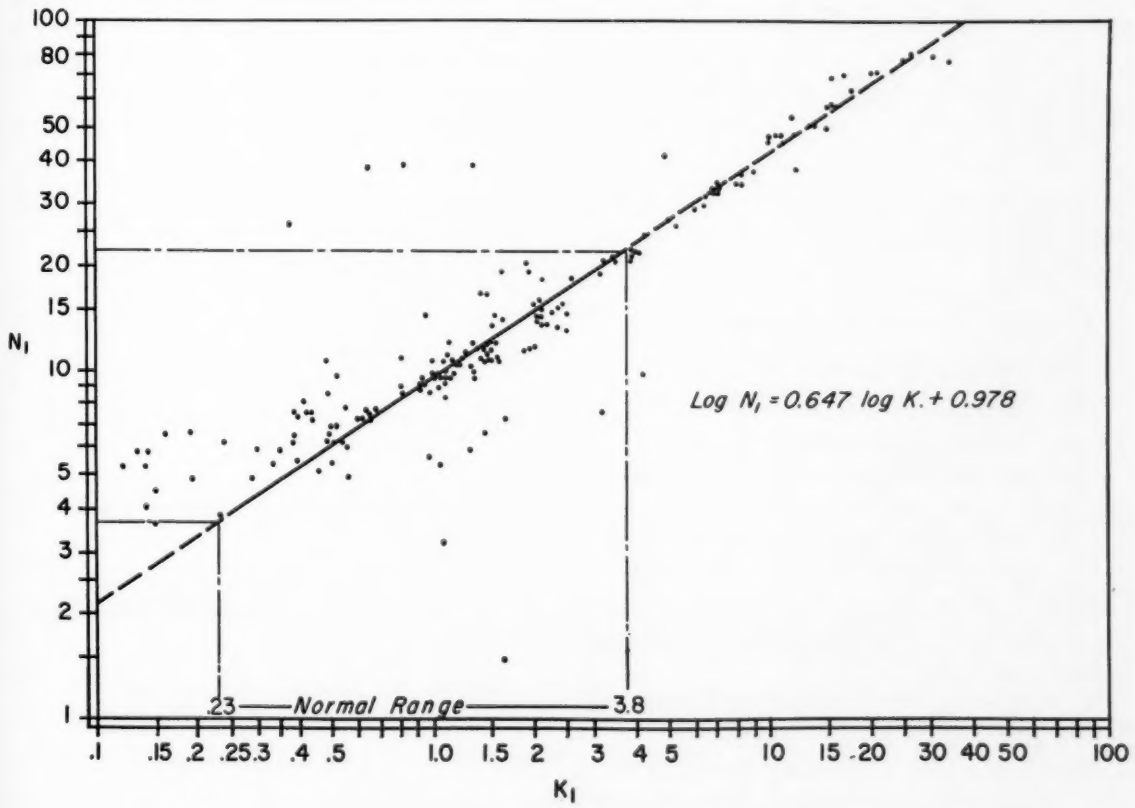

FIG. 3. Log-log relationship of k_1 to N_1 (percentage uptake over thyroid at the end of one hour) by our technique (276 cases).

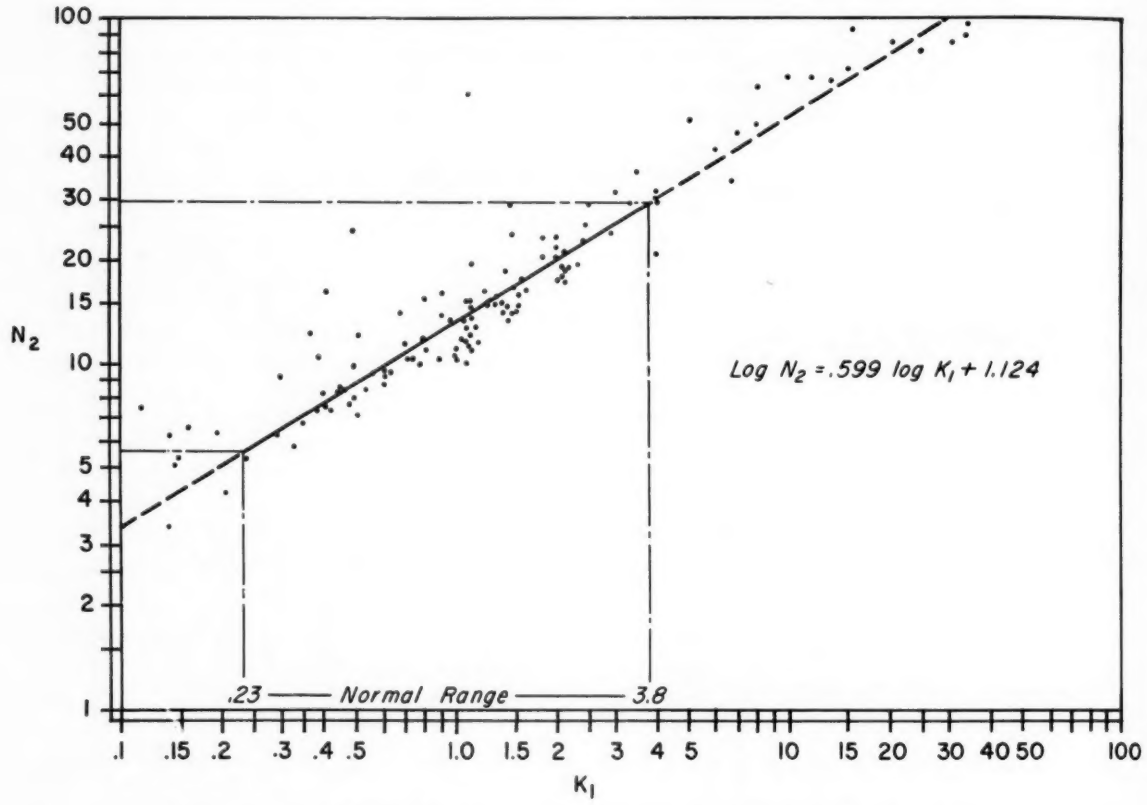

FIG. 4. Log-log relationship of k_1 to N_2 (percentage uptake over thyroid at the end of second hour) by our technique.

first hour (Fig. 3), and N_2 at the end of the second hour (Fig. 4) (with 165 cases), is a linear one. This may be expressed by the formulas:

$$\log N_1 = 0.647 \log k_1 + 0.978 \quad (2)$$

$$\log N_2 = 0.599 \log k_1 + 1.124 \quad (3)$$

The statistical correlation factor is 1.00036 where 1.00000 would be perfect.

The euthyroid range for N_1 includes: 3.7 to 22.5 per cent.

The euthyroid range for N_2 includes: 5.5 to 29.6 per cent.

N_1 values above 22.5 per cent and N_2 values above 29.6 per cent are interpreted as hyperthyroid.

N_1 values below 3.15 per cent and N_2 below 4.75 per cent are hypothyroid.

Borderline values between 3.15 per cent and 3.7 per cent for N_1 and 4.75 per cent to 5.5 per cent for N_2 are difficult to interpret with accuracy—and in these ranges k_1 and k_2 values are helpful particularly for time intervals of four hours or longer (to 24 hours) (Table II).

Also, it is shown that the percentage excretion, E_1, at one hour does not vary significantly in the various thyroid states (Fig. 5).

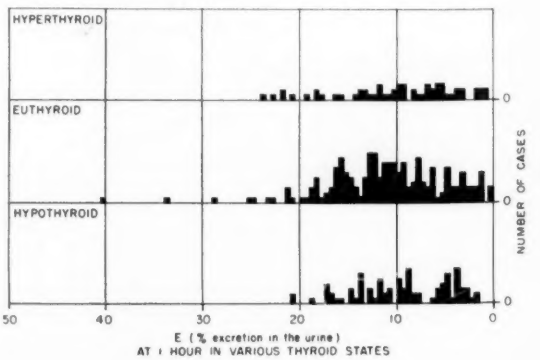

FIG. 5. Bar graph showing similarity of excretion percentage at one hour, E_1 in various thyroid states (276 cases).

DISCUSSION

It is interesting to note that percentage at the end of one hour can be correlated with the k_1 clearance rate factor with such precision. This may be anticipated from the observation that after employing the k_2 (renal rate) factor for a considerable period of time it is noted that the k_1 factor is not modified significantly by k_2.

Even though in the extremely low zone the percentage uptake, N, falls away somewhat from the k_1 factor, the relative accuracy of the determination is usually not impaired. A 24 hour observation period is recommended for these patients in any event.

It is our present feeling, therefore, that the percentage uptake determination at one and/or two hours when employed as we have originally described it, or as we have modified the ORINS technique, is as accurate for clinical application as is our previous k_1 technique determination with the exception of the low hypothyroid zone (less than 5.5 per cent). It is considerably simpler to perform and less time consuming. It is, however, advantageous to employ the intravenous injection of the tracer dose in this test to give one the most accurate type result at the end of one hour.

It is also advantageous to prolong tests on hypothyroid patients for a minimum of four hours when N_2 falls below 5.5 per cent, or as long as 24 hours, and in these patients k_1 determinations are helpful.

In comparing the three log curves—log percentage uptake by ORINS technique, log N_1 and log N_2 (equations 1, 2, and 3 above), it is noted that parallel lines may be obtained in the euthyroid and hyperthyroid zones. This would suggest that the A and B filters serve to depress these percentage uptake values by a constant factor, and that the improvement in accuracy is not significant in the *euthyroid* and *hyperthyroid ranges* since the extra thyroidal percentage contribution to this collimated determination at one and two hours is ordinarily not significant. It may well be significant in the hypothyroid range.

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REFERENCES

1. Oddie, T. H., Meschan, I. and Wortham, J. Thyroid function assay with radioiodine. I. Physical basis of study of early phase of iodine metabolism and iodine uptake. *J. Clin. Investigation*, 1955, *34*, 95–105.
2. Oddie, T. H., Meschan, I., and Wortham, J. Thyroid function assay with radioiodine. II. Routine calculation of thyroidal and renal rate factors. *J. Clin. Investigation*, 1955, *34*, 106–114.
3. Oddie, T. H., Meschan, I., and Wortham, J. Thyroid function assay with radioiodine. III. Clinical test results and diagnostic limits for rate constants. *J. Clin. Investigation*, 1955, *34*, 1044–1056.

THE MEASUREMENT OF SALIVA I^{131} IN PERCENTAGE OF GIVEN DOSE PER LITER AS AN INDEX OF THYROID FUNCTION

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ONE of the more recent tests for the determination of thyroid function is the measurement of the I^{131} activity in the saliva. This test was used in addition to thyroid uptake, conversion ratio and plasma protein bound iodine 131 (PBI^{131}) measurements to differentiate the euthyroid, hyperthyroid and hypothyroid states.

Thode, Jaimet and Kirkwood[7,12] measured the radioactivity of a sample of saliva collected twenty-four hours after a dose of 50 μc of I^{131}. They found that the ratio of this activity to that of plasma and to that of PBI^{131} in the plasma correlated well with hypo- and hyperfunctioning of the thyroid gland. They established norms and ranges for euthyroid, hypothyroid and hyperthyroid states.

Rubenfeld *et al.*[9] measured saliva activity in counts/min./cc. and found this test to be next to the conversion ratio in reliability for the differentiation of thyroid states.

Gabrielsen and Kretchmar[6] found in a series of 13 patients the ratio of salivary I^{131} activity to plasma iodide activity similar in hypothyroid, hyperthyroid and euthyroid patients. They, however, used patients who had had various thyroid procedures and these patients, as had been shown by Silver *et al.*,[11] cannot be classified even by the older methods of uptake and plasma PBI^{131}.

Freinkel and Ingbar,[4] and Fellinger, Hofer and Vetter[2] at first did not corroborate Thode and co-workers' findings. Later Freinkel and Ingbar,[5] using Thode and coworkers' method of collecting saliva, confirmed their results. However, they suggested that the saliva activity chiefly reflects variation in the partition of plasma radioactivity between the iodide and the protein bound fractions rather than intrinsic differences in salivary function.

Our data appear to show that the salivary gland may have a more positive function than that of mere absorption of the iodide radical, for the ratio of salivary activity to total plasma activity or plasma iodide activity or plasma protein bound iodine activity varies in the same patient with time, and varies according to the disease state.

METHOD

Twenty-four and seventy-two hours after a dose of approximately 50 μc of I^{131}, the saliva, plasma and plasma PBI^{131} activities and the uptake were measured. The patient was given a paper cup into which to expectorate. About 5 cc. of saliva was collected. To avoid contamination this cup was placed inside another, which served as a holder. The saliva was stirred to mix the mucus and serous portions, and was pipetted into a plastic test tube marked for a 2 cc. content. Broken off 5 cc. graduated pipettes, which had been fire polished, gave a sufficient bore through which saliva could be pipetted with a rubber bulb. The saliva was measured in a scintillation well counter attached to a spectrometer, the background of which was approximately 30 counts/min. The scaler was calibrated with a known amount of I^{131}. The sensitivity was approximately 600,000 counts/min. per μc for a 2 cc. sample.

The plasma PBI^{131} was obtained by the use of a resin column which is an adaptation by Abbott of methods developed by Scott and Reilly,[10] Zieve, Vogel and Schultz,[13] and Fields and colleagues.[3] The resin column removes the iodide radical and permits the protein bound material to drip through into the test tube with the eluent. Figure 1 illustrates the set-up.

The counts/min./cc. were converted into percentage of given dose per liter, % D/L, thus allowing for direct comparison when the doses given were slightly different and also allowing others to compare their results with ours.

All patients were examined clinically and classified according to thyroid and cardiac function. The groups here reported include euthyroid, hyperthyroid, primary hypothyroid and hypothyroid cases after surgery and/or I^{131} therapy. Euthyroid refers only to patients without past history of thyroid abnormality, hyperthyroid to patients with untreated active thyrotoxicosis.

Fig. 1. Set-up of ioresin columns for protein bound iodine 131 work.

RESULTS

The data for 16 euthyroid patients for twenty-four and seventy-two hours are shown in Table 1: the uptake in column 2; the PBI^{131} in column 3; the inorganic iodide in column 4; the conversion ratio in per cent, *i.e.*, the ratio of PBI^{131} counts to total plasma counts × 100 in column 5. Column 6 contains the total saliva activity measured as percentage of dose per liter. The relationships of saliva activity to various plasma components are shown in the rest of the table. Column 7 gives the saliva to plasma ratio; column 8 the saliva to plasma PBI^{131} ratio; and column 9 the saliva to plasma inorganic iodide ratio. The average for each column is listed at the bottom of the tables. The twenty-four hour average saliva activity in percentage of dose per liter, % D/L, is 8.8.

Although similar data were collected for

Table I

I^{131} uptake, plasma and saliva data for euthyroid patients

1	2		3		4		5		6		7		8		9	
			Plasma						Saliva							
Patient No.	Uptake		PBI^{131} %D/L		Inorganic I^{131} % D/L		Per Cent Conversion Ratio PBI^{131} /Pl. I^{131}		% D/L		S/Pl.		S/Pl.PBI^{131}		S/Pl. Inorganic I^{121}	
	24 hr.	72 hr.	24 hr.	72 hr.	24 hr.	72 hr.	24 hr.	72 hr.	24 hr.	72 hr.	24 hr.	72 hr.	24 hr.	72 hr.	24 hr.	72 hr.
6	31.0	—	.02	.055	.21	.055	8.8	50.7	10.4	.38	43	3.8	482	7.5	47	7.27
9	32.3	32.4	.04	.026	.21	.031	16.0	36.0	10.1	.42	41	—	254	—	50	—
33	50.0	47.3	.034	.134	.19	.024	15.2	85.0	7.1	.38	30.6	2.4	208	2.8	37.2	15.9
35	36.0	37.6	.032	.028	.20	.015	13.9	64.7	8.4	.313	36.2	7.3	262	11.2	42.3	18.3
38	43.5	42.6	.048	.066	.17	.016	22.1	79.5	6.6	.262	30.5	3.2	138	3.97	39.0	15.4
39	44.0	44.5	.074	.097	.14	0	35.3	100	5.6	.361	26.6	4.3	75.7	3.69	41	∞
45	23.6	22.2	.104	.16	.32	0	24.8	100	14.2	.73	33.6	5.0	135	4.6	44.8	∞
46	39.4	37.5	.051	.18	.22	.01	18.8	95	8.6	.70	31.5	3.6	168	3.8	39	67.8
71	32.6	30.9	.038	.065	.311	.008	10.7	89.5	12.2	.596	34.9	8.3	325	9.2	38.9	78
74	31.1	31.3	.044	.075	.151	0	22.6	100	8.01	.128	40.7	2.1	181	1.7	52.7	∞
80	22.0	19.8	.026	.082	.157	0	14.1	100	10.9	.27	59.0	3.3	418	3.3	69.2	∞
84	54.2	52.5	.085	.146	.108	0	44	100	6.2	.48	32	3.6	72.3	3.3	57	∞
85	25.0	21.6	.055	.054	.20	.005	21.5	92	7.5	.37	29	6.3	136	6.8	37.3	76.9
86	22.0	20.7	.034	.039	.287	0	10.7	100	7.1	.23	22	6.3	205	6.0	24.5	∞
110	37.6	35.8	.014	.017	.145	.008	8.5	67.8	7.6	.29	48	11.7	565	17.3	52.2	36.4
132	41.5	40.5	.065	.179	.144	0	31.1	100	9.5	.54	45.3	3.1	145	3.0	65.8	∞
Av.	35.4	34.5	.047	.088	.197	.010	19.9	85.0	8.8	.403	36.5	5.0	235.6	5.88	46.1	

TABLE II

I^{131} UPTAKE, PLASMA AND SALIVA DATA FOR HYPERTHYROID PATIENTS

1	2		3		4		5	6	7	8	9
Patient No.	Uptake		Plasma				Per Cent Conversion Ratio PBI^{131}/Pl. I^{131}	Saliva			S/Pl. Inorganic I^{131}
			PBI^{131}% D/L		Inorganic I^{131}% D/L			% D/L	S/Pl.	S/Pl. PBI^{131}	
	24 hr.	72 hr.	24 hr.	72 hr.	24 hr.	72 hr.	24 hr.	24 hr.	24 hr.	24 hr.	24 hr.
20	81	73	.72	1.27	0	.007	100	2.23	3.1	3.1	∞
24	53.5	50.8	.076	.19	.018	0	81.2	1.01	10.8	13.2	46
26	46.3	34	.58	1.19	0	0	100	1.48	2.6	2.5	44.4
29	88	75	1.17	1.60	0	.27	100	1.89	1.65	1.6	9.5
43	94	80.7	.59	1.32	.055	.06	91.4	.26	.41	.45	4.8
61	77	71	.334	.74	.083	.123	89.5	1.4	3.74	4.2	35.2
81	71	56.1	1.68	1.94	.148	.196	92	1.96	1.07	1.17	13.2
95	72	62.1	1.57	2.41	.336	.336	82	.95	.50	.60	2.8
101	84.5	75	.713	1.33	.109	.137	87	1.4	1.7	1.98	13
104	70.5	54.5	1.72	2.50	.122	.110	93.5	.66	.36	.38	5.4
113	67.6	62.5	.530	.844	.045	.118	92	1.4	2.6	2.9	33.2
114	59.8	56.0	.147	.369	.111	.018	57.2	4.8	18.5	32.3	43.2
126	88	73.3	.85	2.04	.049	.27	94.4	.95	1.06	1.12	19.5
133	90	72	.55	1.29	.013	.035	98	1.2	2.1	2.2	89.5
Av.	74.5	64.0	.802	1.36	.077	.120	89.9	1.54	3.59	4.84	

all patients, the seventy-two hour columns on saliva data and on the conversion ratio are omitted from subsequent tables because these data do not help in differentiating the different disease states of the thyroid.

The values for 14 hyperthyroid patients are found in Table II. The average concentration of salivary I^{131} is only 1.54 % D/L, whereas this value in the euthyroid is 8.8 %. This decreased salivary activity and increased plasma activity in the hyperthyroid group reduces the saliva to plasma ratio from 36.5 in the euthyroid to 3.6 in the hyperthyroid. The average ratio of saliva to plasma PBI^{131} is 236 in the euthyroid and 4.8 in the hyperthyroid.

The data for 8 primary hypothyroid patients are found in Table III. The levels of plasma PBI^{131} are not helpful in confirming the diagnosis. However, the conversion ratio is depressed because of the large amount of circulating inorganic iodide still present in the plasma twenty-four hours after administration of the tracer. The most striking finding in these patients is the greatly increased salivary activity. The average is 32 % D/L as compared to 8.8 % in the euthyroid. The saliva to plasma PBI^{131} ratio is also greatly increased over that of the euthyroid, 1,029 as compared to 236.

Table IV contains data on patients who became hypothyroid after either surgical or I^{131} thyroidectomy. The uptake and conversion ratios are similar to those in the primary hypothyroid group of Table III. However, in the former patients the plasma PBI^{131} values are higher. Silver *et al.*[11] showed this increase in plasma PBI^{131} in thyroidectomized patients.

Figures on patients who were clinically euthyroid at the time of the tracer study but who had had either thyroid surgery or

TABLE III

I^{131} UPTAKE, PLASMA AND SALIVA DATA FOR PRIMARY HYPOTHYROID PATIENTS

1	2		3		4		5	6	7	8	9
			Plasma					Saliva			
Patient No.	Uptake		PBI^{131}% D/L		Inorganic I^{131}% D/L		Per Cent Conversion Ratio PBI^{131}/Pl. I^{131}	% D/L	S/Pl.	S/Pl. PBI^{131}	S/Pl. Inorganic I^{131}
	24 hr.	72 hr.	24 hr.	72 hr.	24 hr.	72 hr.	24 hr.	24 hr.	24 hr.	24 hr.	24 hr.
51	10.4	1.4	.051	.043	1.64	.18	3.9	42.0	24.6	633	25.6
52	10.5	—	.087	.049	1.64	.30	6.4	47.0	26.8	417	28.6
65	10.1	5.0	.058	.060	.845	.061	6.4	29.4	32.4	502	34.5
141	17.2	13.7	.058	.032	.640	.021	8.3	25.0	35.7	433	39.0
164	29.2	—	.016	—	.213	—	7.2	14.8	64.6	895	69.3
165	26.2	—	.033	—	.332	—	9.1	24.6	67.5	738	74.2
174	13.7	—	.014	—	.460	—	2.9	46.7	98.5	3370	101.0
179	19.5	—	.019	—	.356	—	5.1	23.5	62.8	1240	66.2
Av.	17.1	6.7	.042	.046	.765	.140	6.2	31.6	51.6	1029	54.8

previous treatment with I^{131} are given in Table v. Here again the plasma PBI^{131} and the plasma inorganic iodide values are high, although the uptake and conversion ratio figures are normal. The saliva activity has increased to 24.5 % D/L from 8.8 for the euthyroid. These findings represent confirmation of Silver and co-workers' observations that the metabolism of I^{131} remains altered in the partially thyroidectomized individual.

In order better to follow the distribution of I^{131} after oral administration, the saliva activity and uptake were measured hourly

TABLE IV

I^{131} UPTAKE, PLASMA AND SALIVA DATA FOR HYPOTHYROID PATIENTS AFTER SURGERY AND/OR I^{131} THERAPY

1	2		3		4		5	6	7	8	9
			Plasma					Saliva			
Patient No.	Uptake		PBI^{131}% D/L		Inorganic I^{131}% D/L		Per Cent Conversion Ratio PBI^{131}/Pl. I^{131}	% D/L	S/Pl.	S/Pl. PBI^{131}	S/Pl. Inorganic I^{131}
	24 hr.	72 hr.	24 hr.	72 hr.	24 hr.	72 hr.	24 hr.	24 hr.	24 hr.	24 hr.	24 hr.
108	11.2	6.6	.021	.148	.328	.018	6.0	16.4	46.8	780	49.8
128	8.7	4.0	.058	.076	.490	.027	10.6	45.6	83.5	823	93.0
148	17.9	13.9	.101	.244	.54	.047	15.7	44.2	68.8	440	81.5
150	30.4	33.0	.036	.052	.53	.002	6.4	52.3	93.0	1460	99.5
Av.	17.1	14.4	.054	.130	.472	.023	9.7	39.6	73.0	876	80.9

TABLE V

I^{131} UPTAKE, PLASMA AND SALIVA DATA FOR EUTHYROID PATIENTS AFTER SURGERY OR I^{131} THERAPY

1	2		3		4		5	6	7	8	9
			Plasma					Saliva			
Patient No.	Uptake		PBI^{131} % D/L		Inorganic I^{131} % D/L		Per Cent Conversion Ratio PBI^{131}/Pl. I^{131}	% D/L	S/Pl.	S/Pl. PBI^{131}	S/Pl. Inorganic I^{131}
	24 hr.	72 hr.	24 hr.	72 hr.	24 hr.	72 hr.	24 hr.	24 hr.	24 hr.	24 hr.	24 hr.
7		16.8	.04	.058	.72	.028	4.6	37.6	50.4	1090	56.2
44	11.1	6.0	.079	.153	.45	.022	14.8	30.2	56.5	383	66.4
47	28.6	28.0	.049	.084	.177	0	21.6	18.9	81.5	377	104
49	18.5	11.8	.306	.60	.745	.013	29.2	33.2	31.6	108	44.8
57	57.5	59.0	.097	.183	.255	.009	27.4	8.17	23.1	84.5	31.7
63	36.2	31.5	.09	.368	.180	.004	33.7	13.1	48.7	144	73.3
64	28.4	28.6	.013	.026	.119	.012	10.1	10.6	80.0	790	88.9
68	24.6	18.2	.130	.291	.802	.034	14.1	54.7	58.2	412	67.9
79	31.0	27.3	.055	.170	.198	.017	21.9	7.35	29.2	133	37.3
89	40		.51		.76		40.2	38.3	30.5	76	51.1
112	21.8	15.5	.189	.412	.915	0	17.1	41.7	41.2	242	49.8
115	38.5	39.0	.037	0	.37	.025	9.1	15.1	37.0	405	40.8
117	19.6	15.1	.091	.20	.47	.04	16.0	23.8	42.1	263	50
127	43.8	42.3	.157	.070	.097	.022	61.3	10.1	39.9	65.2	19.5
Av.	30.7	26.1	.131	.201	.447	.017	22.9	24.5	46.4	326.6	55.8

in one patient for eight hours and then at twenty-four hours. These are plotted in Figure 2. In another patient in addition to the saliva activity and uptake, the plasma and plasma PBI^{131} activities were also determined. The results are plotted in Figure 3. Both patients had had total surgical thyroidectomies for carcinoma of the thyroid. The saliva activity increased for four hours, decreased sharply during the next hour and then after a slight rise decreased from 50 to 20 % D/L by twenty-four hours. In Figure 3 the saliva activity increased for six hours, fell sharply for two hours and decreased to about half during the next eighteen hours. The change in the plasma iodide during this time is shown on the graph. The saliva activity does not parallel the plasma iodide during the first eight hours. In column 9 of Table I are listed the ratios of saliva to plasma inorganic iodide activity. The seventy-two hour ratios are not the same as the twenty-four hour ratios; in some instances they are larger and in some instances smaller. Therefore it does not seem that the salivary gland merely absorbs a certain percentage of the available iodide in the plasma.

DISCUSSION

A summary of the results of all tests is given in Tables VI and VII and a comparison with the results of Thode *et al.* is made in Table VIII. There is a distinct difference in the total salivary activity expressed as percentage of dose per liter, % D/L, between euthyroid, hyperthyroid and hypothyroid patients. In each group the ranges do not overlap those in the other disease states.

The S/Pl.PBI^{131} ratios are also considerably different between euthyroid, hyperthyroid and hypothyroid states with very little overlapping. This ratio does not ap-

Table VI

COMPARISON OF AVERAGE AND RANGE OF I^{131} UPTAKE AND PLASMA DATA IN VARIOUS DISEASE STATES

Disease State	No. of Patients	Uptake		Pl. PBI^{131} % D/L				Pl. Inorganic I^{131} % D/L				Per Cent Conversion Ratio $PBI^{131}/Pl.I^{131}$	
		24 hr.		24 hr.		72 hr.		24 hr.		72 hr.		24 hr.	
		Av.	Range	Av.	Range	Av.	Range	Av.	Range	Av.	Range	Av.	Range
Euthyroid	16	35.4	22.0–54.2	.047	.014–.104	.088	.017–.180	.197	.108–.320	.010	0–.055	19.9	8.5–44.0
Hyperthyroid	14	74.5	46.3–94.0	.802	.076–1.72	1.36	.190–2.50	.077	0–.336	.120	0–.336	89.9	57.2–100
Primary Hypothyroid	8	17.1	10.1–29.2	.042	.014–.087	.046	.032–.060	.765	.213–1.64	.140	.021–.30	6.2	2.9–9.1
Hypothyroid after I^{131} or Surgery	4	17.1	4.0–33.0	.054	.021–.101	.130	.052–.244	.472	.328–.540	.023	.002–.047	9.7	6.0–15.7
Euthyroid after I^{131} or Surgery	14	30.7	11.1–57.5	.131	.013–.510	.201	0–.412	.447	.097–.915	.017	0–.04	22.9	4.6–61.3

Table VII

COMPARISON OF THE 24 HOUR AVERAGE AND RANGE OF SALIVA I^{131} DATA IN VARIOUS DISEASE STATES

Disease State	No. of Patients	Saliva % D/L		S/Pl.		S/Pl. PBI^{131}		S/Pl. Inorganic I^{131}	
		Av.	Range	Av.	Range	Av.	Range	Av.	Range
Euthyroid	16	8.8	5.6–14.2	36.5	22.0–59.0	235.6	72.3–565	46.1	24.5–69.2
Hyperthyroid	14	1.54	.66–4.8	3.59	.36–18.5	4.84	.38–32.3		2.8–∞
Primary Hypothyroid	8	31.6	14.8–47.0	51.6	24.6–98.5	1029	417–3370	54.8	25.6–101
Hypothyroid after I^{131} or Surgery	4	39.6	16.4–52.3	73.0	46.8–93.0	876	440–1460	80.9	49.8–99.5
Euthyroid after I^{131} or Surgery	14	24.5	7.35–54.7	46.4	23.1–81.5	326.6	65.2–1090	55.8	19.5–104

Table VIII

COMPARISON OF I^{131} RESULTS WITH THOSE OF THODE AND CO-WORKERS[12]

Test		Euthyroid		Hyperthyroid		Hypothyroid	
		Av.	Range	Av.	Range	Av.	Range
Uptake	Present Authors	35.4	22.0–54.2	74.5	46.3–94.0	17.1 17.1	10.1–29.2 Primary 4.0–33.0 Secondary
	Thode and Co-workers	28	18–35	76	42–91	11.7	1.8–29.2
Conversion Ratio	Present Authors	19.9	8.5–44.0	89.9	57.2–100	6.2 9.7	2.9–9.1 Primary 6.0–15.7 Secondary
	Thode and Co-workers	17	11–23	80	45–100	9.1	2.5–16.0
S/Pl. PBI^{131}	Present Authors	235.6	72.3–565	4.84	.38–32.3	1029 876	417–3370 Primary 440–1460 Secondary
	Thode and Co-workers	188	160–235	10.4	.25–40	879	338–3200

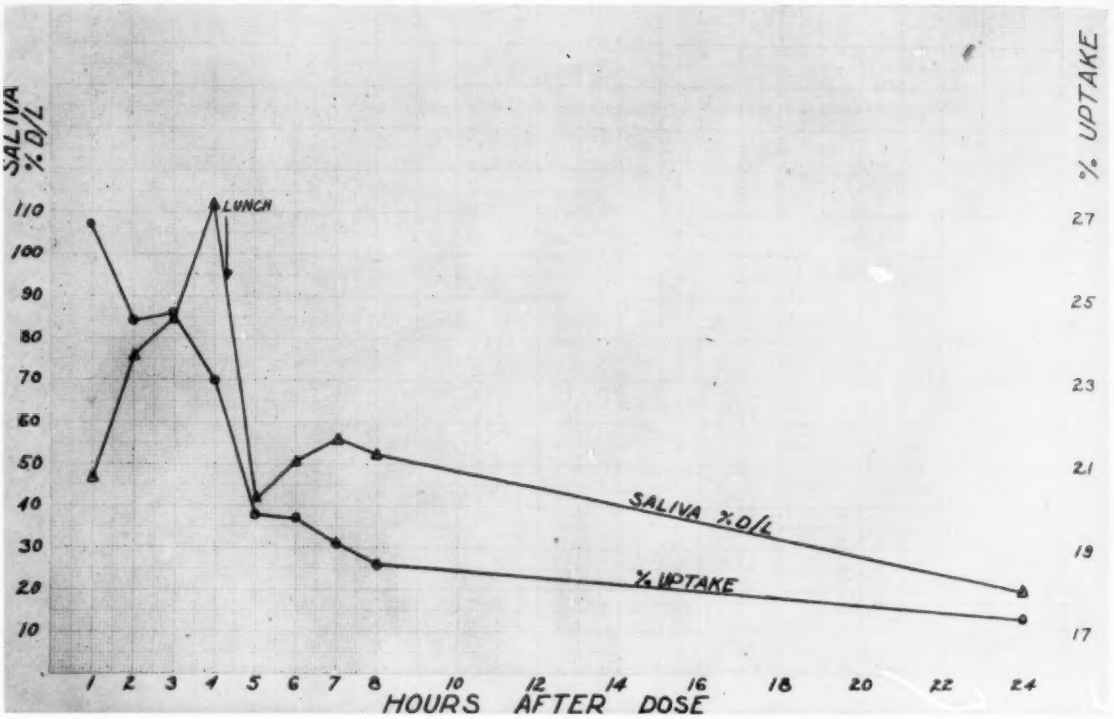

FIG. 2. Graphs of total saliva activity plotted as percentage of given dose per liter, % D/L, versus time after dose for patient No. 108, Table IV. Carcinoma of thyroid, hypothyroid after surgery.

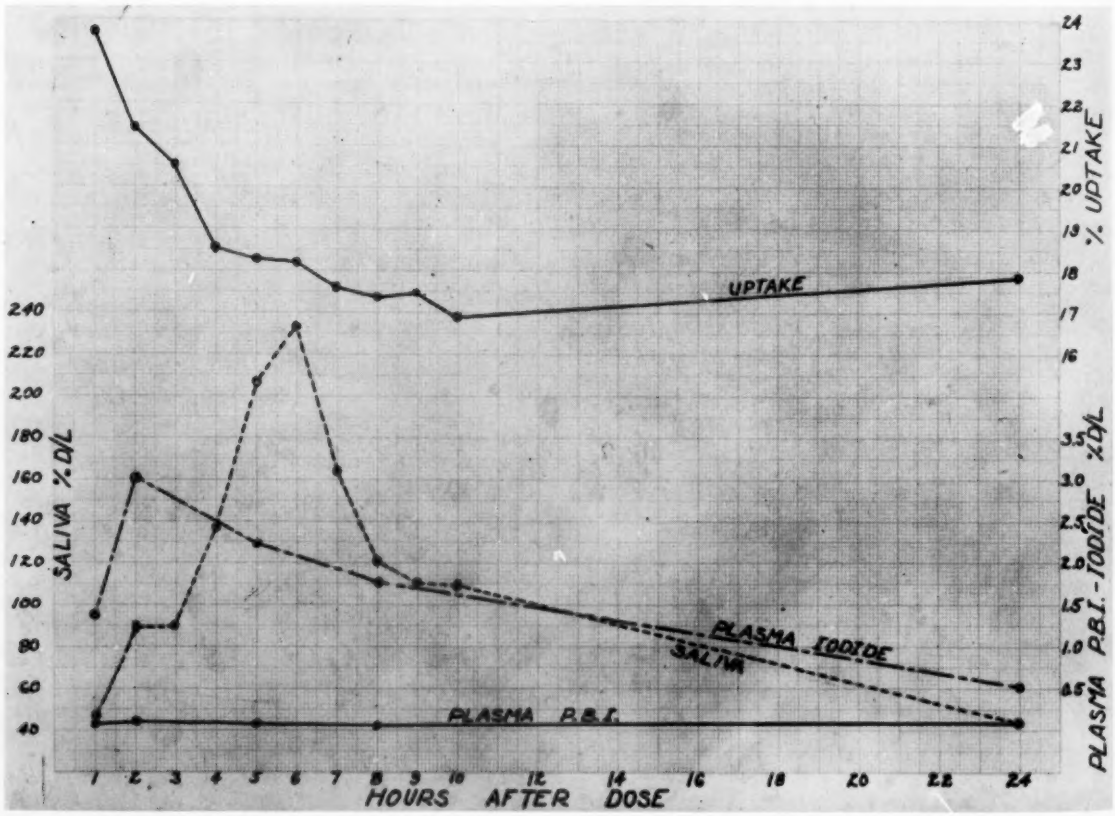

FIG. 3. Graphs of total saliva activity and plasma protein bound iodine 131 activity plotted as % D/L versus time after dose for patient No. 148, Table IV. Carcinoma of thyroid, hypothyroid after surgery.

pear to be a better index than that of saliva activity expressed as % D/L.

The average saliva activity for the hyperthyroid group is 1.54 % D/L, compared to 8.8 % D/L in the euthyroid, with a range from .66 to 4.8. This low concentration of I^{131} in saliva seems to be found only in hyperthyroidism.

It is not the euthyroid hyperthyroid border which is difficult to delineate, but the euthyroid hypothyroid margin. Here the seventy-two hour plasma PBI^{131} value fails to differentiate the mildly or even moderately hypothyroid from the normal individual. The uptake is not always definitive. A low conversion ratio, high saliva activity in the range of 15 to 50 % D/L and a high S/Pl.PBI^{131} ratio in the range of 400 to 3,000 are indicative of hypothyroidism.

The measurement of total saliva activity as % D/L appears to be one of the simplest methods of separating the hypothyroid from the euthyroid. However, one should be cognizant of the fact that patients with congestive heart failure[1,8] may give values similar to the hypothyroid patient for all of these indices except the uptake.

SUMMARY

1. The uptake, total plasma, plasma PBI^{131} and total saliva activity were measured at twenty-four and seventy-two hours in 56 patients.

2. The patients were classified clinically. Tables are given of the twenty-four and seventy-two hour measurements and ratios calculated from these values for euthyroid patients.

3. Tables are given of the twenty-four hour saliva measurements and ratios, and the conversion ratio; and the twenty-four and seventy-two hour uptake, plasma PBI^{131} and inorganic iodide values, in hyperthyroid, primary hypothyroid, hypothyroid after surgery or I^{131} therapy and euthyroid after thyroid surgery or I^{131} therapy.

4. Comparisons of the values and the ranges are tabulated for the various groups.

5. The variation of saliva and uptake with time for a twenty-four hour period is plotted for one patient; and saliva, uptake, plasma PBI^{131} and plasma inorganic iodide for another patient.

6. The total saliva activity is highest in the hypothyroid groups, and lowest in the hyperthyroid group, with 36 % D/L as an average for the former, 1.5 % D/L for the latter and 8.8 % D/L for the euthyroid group.

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REFERENCES

1. Birkhill, F. R., Corrigan, K. E., and Hayden, H. S. Metabolism of radioactive iodine (I^{131}) in patients with cardiac disease. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1952, *67*, 42–50.
2. Fellinger, K., Hofer, R., and Vetter, H. Salivary and thyroidal radioiodide clearances of plasma in various states of thyroid function. *J. Clin. Endocrinol. & Metab.*, 1956, *16*, 449–461.
3. Fields, T., Kinnary, D. S., Kaplan, E., Oester, Y. T., and Bowser, E. Determination of protein-bound iodine^{131} with anion exchange resin column. *J. Lab. & Clin. Med.*, 1956, *47*, 333–336.
4. Freinkel, N., and Ingbar, S. H. Concentration gradients for inorganic I-131 and chloride in mixed human saliva. *J. Clin. Invest.*, 1953, *32*, 1077–1084.
5. Freinkel, N., and Ingbar, S. H. Further observations concerning salivary transport of iodide. *New England J. Med.*, 1955, *252*, 125–127.
6. Gabrielsen, Z., and Kretchmar, A. L. Studies on salivary secretion of iodide. *J. Clin. Endocrinol. & Metabol.*, 1956, *16*, 1347–1353.
7. Jaimet, C. H., and Thode, H. G. Further clinical studies of thyroid and salivary gland function with radioiodine. *Canad. M. A. J.*, 1956, *74*, 865–870.
8. Mescham, I., Oddie, T. H., Wortham, J. T., Doherty, J. E., and Little, E. Correlation of iodine 131 clearance rate factors with cardiac functional status, protein-bound-iodine plasma values, and blood nonprotein

nitrogen. AM. J. ROENTGENOL., RAD. THERAPY & NUCLEAR MED., 1957, *77*, 847–851.

9. RUBENFELD, S., BRODIE, S., MITCHELL, N., LOWENTHAL, M., and KOHN, A. Radioiodine profile in diagnosis of thyroid disease. *A.M.A. Arch. Int. Med.*, 1957, *100*, 266–271.
10. SCOTT, K. G., and REILLY, W. A. Use of anionic exchange resin for determination of protein-bound I^{131} in human plasma. *Metabolism*, 1954, *3*, 506–509.
11. SILVER, S., YOHALEM, S. B., and NEWBURGER, R. A. Pitfalls in diagnostic use of radioactive iodine. *J.A.M.A.*, 1955, *159*, 1–5.
12. THODE, H. G., JAIMET, C. H., and KIRKWOOD, S. Studies and diagnostic tests of salivary gland and thyroid gland function with radioiodine. *New England J. Med.*, 1954, *251*, 129–134.
13. ZIEVE, L., VOGEL, N., and SCHULTZ, A. Determination of protein bound radioiodine with anion exchange resin. *Clin. Research*, 1955, *3*, 120.

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THE USE OF RADIOACTIVE ISOTOPES IN THE STUDY OF COLONIC ABSORPTION*

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IT HAS long been known that the colonic mucosa can preferentially absorb certain materials. Annis and Alexander[1] in 1952 demonstrated that the human sigmoid colon absorbed chloride in preference to sodium by a ratio of 2–7 to 1. This was demonstrated again in dogs by D'Agostino *et al.*[2] in 1953 and the replacement of the chloride by carbonate ion was pointed out. It was also suggested by this group that a gradient between sodium and potassium ions existed at a lower level.

The net absorption has been found to decrease in white rats when a strongly hypertonic solution is used, yet the concentration of sodium and chloride ions in a hypotonic solution has been known to decrease further due to absorption.[3] These findings indicate that absorption may take place from the colon regardless of osmotic pressures present and that the colonic mucosa does active work.

In patients with ureterosigmoidostomies and kidney failure, the absorption of chloride ion from the colon has been found to take place even though the patient has a marked hyperchloremia.[4] This demonstrates that the blood level of the ion, at least in the case of chloride, does not exert a great deal of control over the colonic mucosal action.

In 1956 Joske and Sherriff[5] found the absorption of I^{131}, as iodine ion, from the Gilchrist bladder made from the right colon in man to be 13–52 per cent. They measured both the blood radioactivity and the amount recovered from the bladder.

In view of the above findings, it might be possible to evaluate the integrity of the colonic mucosa by the use of radioactive labeled materials. With this in mind the following study was undertaken.

METHODS AND MATERIALS

This study consisted of two parts, one pertaining to humans and the other pertaining to dogs.

Study of Humans. Patients seen in the radiology department for barium examinations of the colon were divided into four groups, each of which was given a different iodine 131 labeled material. These materials were I^{131} as sodium iodide, I^{131} labeled oleic acid, I^{131} labeled glycerol trioleate, and I^{131} labeled human serum albumin. These various substances were introduced per rectum along with the barium solution. After the procedure these groups of patients were again subdivided as to normal or abnormal, according to barium enema studies.

The material amounting to 2 ml. in volume, and 10 to 15 microcuries in activity was injected through the wall of the barium enema tube, containing a small amount of barium solution. A size 24 hypodermic needle was used and the puncture was made at a point about 10 inches from the distal end of the tube. This procedure was carried out immediately before the barium enema examination. The colon was visualized at fluoroscopy and indicated roentgenographic examinations were carried out. A 2 cc. sample of venous blood was obtained at fifteen minutes after the start of the procedure. The patient was then allowed to evacuate, a postevacuation roentgenogram was made, and another blood sample was obtained. The second sample was taken at thirty minutes after injection. In most cases an additional blood sample at sixty minutes was also obtained. These blood samples were then subjected to radioanalysis. The total blood radioactivity was determined (using 7.2 per cent of the body weight as

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the total blood mass) and this in turn was converted to percentage of administered dose.

Study of Dogs. Dogs were divided into four groups according to the materials which they received. All dogs were anesthetized with sodium pentobarbital intravenously. An enema preparation amounting in volume to 90 cc. was prepared. Initially this preparation contained barium sulfate in concentration sufficient for roentgenographic visualization and there was no ileal reflux observed. Blood samples were taken at ten, twenty, and thirty minutes after injection of material in the fashion similar to that of the human subjects. Radioanalysis was carried out and assuming 7.5 per cent of body weight to represent the total blood mass, the activity present in the total blood volume was determined.

RESULTS

In the groups of humans, both normal and abnormal, we were unable to demonstrate definite evidence of absorption of the labeled oleic acid, glycerol trioleate or human serum albumin. There was evidence in every case that absorption of the ionic iodine had taken place. The results of the findings are shown in Table I.

TABLE I

PERCENTAGE OF ADMINISTERED RADIOACTIVITY PRESENT IN THE TOTAL BLOOD VOLUME AT THE STATED TIME AFTER ADMINISTRATION TO NORMAL HUMANS

Material	15 Min.	30 Min.	60 Min.	90 Min.
Sodium Iodide (I^{131})				
No. of Observations	14	12	15	
Average Values	6.21	6.88	6.91	
Standard Deviation	3.12	2.87	2.97	
Oleic Acid (Labeled with I^{131})				
No. of Observations	1	7	6	4
Average Values	0	0	0	0
Glycerol Trioleate (Labeled with I^{131})				
No. of Observations	6	6	6	
Average Values	0	0	0	
Human Serum Albumin (Labeled with I^{131})				
No. of Observations	14	14	13	
Average Values	0	0	0	

TABLE II

PERCENTAGE OF ADMINISTERED RADIOACTIVITY PRESENT IN THE TOTAL BLOOD VOLUME IN PATIENTS WITH ULCERATIVE COLITIS

Patient	Material	15 Min.	30 Min.
H. H.	Sodium Iodide (I^{131})	0.9	1.2
T. R.		0.6	2.0
G. L.		2.8	3.4
D. B.		1.0	1.9
O. F.		2.7	2.5
Average		1.60	2.20
B. H.	Oleic Acid (I^{131})	0	0
I. P.	Glycerol Trioleate (I^{131})	0	0

The results in the group of patients with chronic ulcerative colitis are presented in Table II, and the results of patients showing partial filling are shown in Table III.

The results obtained in dogs are given in Table IV. It is to be noted that there was some absorption of all of the materials from dog colons with the exception of oleic acid.

DISCUSSION

It may be noted that in the humans only the absorption of iodine was found to take place from the colon to any degree. It should also be noted that in those persons with normal barium enema examinations the average percentage of administered dose in the blood was higher than in those persons with chronic colon disease, specifically chronic ulcerative colitis. It is apparent that this procedure or one similar to it might prove to be quite useful in evaluating the colonic mucosa; however, definite follow-up studies need to be done.

The larger sized molecules were not absorbed to any extent in the human colon. The relative lack of ion formation in these substances might also have been an important factor in the failure of their absorption.

TABLE III

PERCENTAGE OF ADMINISTERED RADIOACTIVITY PRESENT IN THE TOTAL BLOOD VOLUME IN PATIENTS WITH PARTIALLY FILLED COLONS

Patient	Portion of Bowel Visualized	Material	15 Min.	30 Min.	60 Min.
J.R.	Ascending, transverse, descending	Sodium Iodide (I^{131})	—	5.2	5.6
M.M.	Ileum, transverse, descending, sigmoid, rectum	Sodium Iodide (I^{131})	8.8	—	9.0
L.W.	Rectum	Sodium Iodide (I^{131})	1.5	3.7	3.7
O.M.	Ileum, descending, sigmoid, rectum	Sodium Iodide (I^{131})	2.1	3.1	—

We are not prepared at this time to discuss the reason for the differences in the dog and human colonic absorption. When the first dogs were studied under fluoroscopy, it was found that 90 cc. of barium solution did not reflux into the small bowel. This fact should eliminate the possibility of the absorption from the ileum.

It is of some interest that in the dog there was slight but definite absorption of the human serum albumin and of the glycerol trioleate from the colon; however, there was no absorption of the oleic acid. This curiosity we can attribute neither to molecular size nor to ionizability. This difference again points to the self-determination of the colonic mucosa and its ability to absorb at its own discretion.

SUMMARY

A study of absorption of various radioactive labeled substances from normal human and dog colons is presented. It was found that the human colons with widespread mucosal disease absorbed some substances less well than did the colons with a normal mucosa. It is possible that this procedure might offer a new approach to the evaluation of colonic mucosa.

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TABLE IV

PERCENTAGE OF ADMINISTERED RADIOACTIVITY PRESENT IN THE TOTAL BLOOD VOLUME OF NORMAL DOGS

Material	15 Min.	30 Min.	60 Min.	90 Min.	120 Min.
Sodium Iodide (I^{131})					
No. of Observations	10	10	10	10	9
Average	4.74	6.18	7.23	8.10	7.83
Standard Deviation	1.57	1.92	2.29	2.39	2.24
Oleic Acid (I^{131} Labeled)					
No. of Observations	—	7	6	4	—
Average	—	0	0	0	—
Standard Deviation	—	0	0	0	—
Glycerol Trioleate (I^{131} Labeled)					
No. of Observations	15	15	15	15	11
Average	0.34	0.49	0.69	0.83	0.92
Standard Deviation	0.17	0.20	0.19	0.25	0.31
Human Serum Albumin (I^{131} Labeled)					
No. of Observations	17	17	17	9	10
Average	1.30	1.50	2.36	3.68	3.28
Standard Deviation	1.97	2.05	2.38	2.80	2.94

REFERENCES

1. ANNIS, D., and ALEXANDER, M. K. Differential absorption of electrolytes from large bowel in relation to ureterosigmoid anastomosis. *Lancet*, 1952, *2*, 603–606.
2. D'AGOSTINO, A., LEADBETTER, W. F., and SCHWARTZ, W. B. Alterations in ionic composition of isotonic saline solution instilled into colon. *J. Clin. Invest.*, 1953, *32*, 444–448.
3. BUDOLFSEN, S. E. Absorption of sodium chloride in colon and distal part of small intestine. *Acta physiol. scandinav.*, 1954, *32*, 148–162.
4. CREEVY, C. D., and REISER, M. P. Observations upon absorption of urinary constituents after ureterosigmoidostomy: importance of renal damage. *Surg., Gynec. & Obst.*, 1952, *95*, 589–596.
5. JOSKE, R. A., and SHERRIFF, E. V. Method for determination of rate of transfer of I 131 across human colonic mucosa. *Australian & New Zealand J. Surg.*, 1956, *25*, 315–316.

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TREATMENT OF PTERYGIUM BY SURGERY FOLLOWED BY BETA RADIATION*

AN ANALYSIS OF 256 CASES

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THE treatment of pterygia by surgical excision followed by beta-ray application has proved eminently successful. This report aims to document such a five year experience in Bellevue Hospital where 256 patients were observed and treated.

This study represents the largest number of pterygia cases treated by surgery followed by irradiation reported from any one center to date.[2,3,8]

PHYSICAL DATA

Initially in the series, beta-ray therapy was given with a radon applicator. This applicator contained 10 mc of radon enclosed in minute glass capillary tubes, held in a small wooden block. The block with five small grooves, into which the radon tubes fitted, was dipped into paraffin to hold the tubes secure. A detailed description of this applicator has been given by Kaplan.[4] The average radon glass tube wall thickness was about 0.2 mm. which permitted 86 per cent beta-ray emission. The additional wax coating of approximately 0.5 mm. reduced the average output to 70 per cent of the available beta rays. These figures are obviously approximate because of the lack of uniformity of the glass wall thickness and the paraffin deposition.

The radon applicator presents the following disadvantages, as pointed out by Friedell, Thomas, and Krohmer:[2] (1) Radon requires replacement because of its rapid decay (half life 3.82 days); (2) protection against gamma radiation, although not a difficult problem, must be exercised; (3) the glass capsules containing the radon are found to vary in thickness so that calibration by means of the gamma rays emitted does not accurately reflect the beta-ray dosage.

A further disadvantage is that a ten minute treatment time with radon application is often difficult to complete because of poor eye immobilization. Furthermore, personnel must be at an adequate distance to minimize exposure.

In 1953, a strontium 90 applicator containing 50 mc was introduced. Its original emission was 42 rep/sec. at the surface (Fig. 1).

Strontium 90 has a half life of 19.5 plus or minus 0.3 years. Strontium 90 is in equilibrium with yttrium 90, its daughter decay product. It is a pure beta-ray emitter. A small amount of bremsstrahlung results. Strontium 90 is a fission product. In

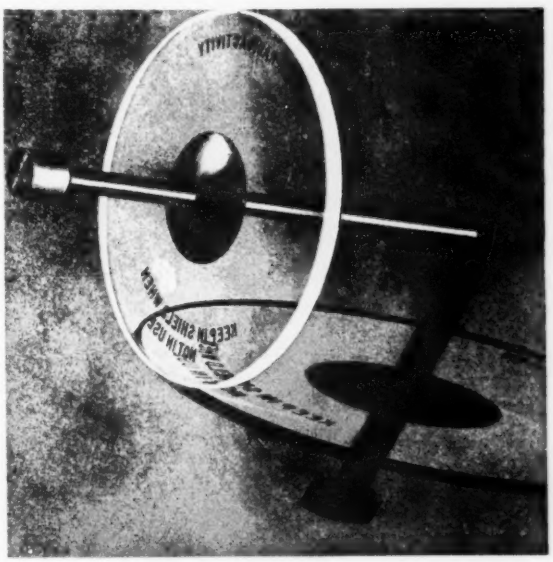

FIG. 1. Photograph of the strontium 90 eye applicator.

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† Deceased.

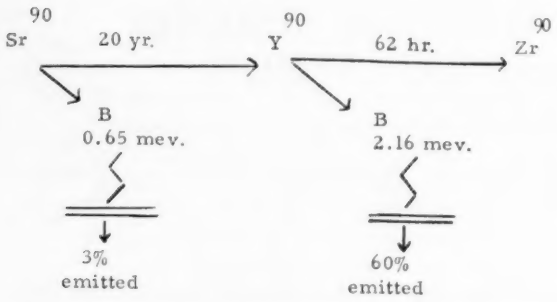

FIG. 2. Diagram illustrating the disintegration scheme and beta-ray emission of the strontium 90 applicator. The combined filter of 0.002 mm. steel and 0.01 mm. aluminum permits transmission of only 3 per cent of the strontium 90 beta activity and 60 per cent of the more energetic yttrium 90 activity.

its decay, it emits a beta-ray particle of 0.65 mev. to become yttrium 90. Yttrium 90 with a half life of 62 hours emits a beta particle of 2.16 mev. to form the stable isotope zirconium 90.

The applicator is supplied with a face filter of 0.002 mm. stainless steel plus 0.01 mm. aluminum to yield an effective cover of approximately 100 mg./cm.^{2}.[7]

This filter reduces the number of beta-ray particles from the disintegration of Sr^{90} to about 3 per cent and from the decay of Y^{90} to about 60 per cent. Essentially, therefore, the beta-ray particles emitted from this plaque have the characteristics of a pure Y^{90} spectrum after passing through 100 mg./cm.^{2} of filtration (Fig. 2).

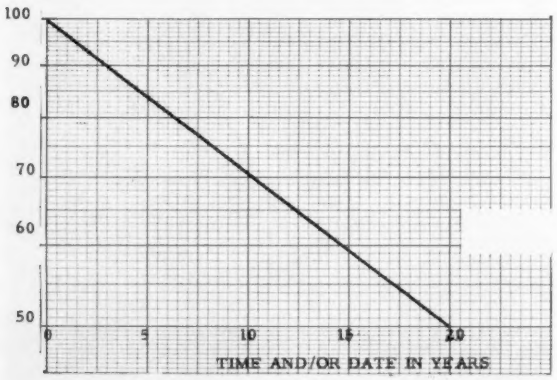

FIG. 3. Curve indicating the twenty year half life of strontium 90. The surface dose rate can be determined at any time after an initial output is measured. (Reproduced by permission from the *Tracerlab Instruction Manual.*)

The decay can be rapidly determined by reference to Figure 3, which shows the twenty year decay curve. The curve also can be used to determine the correction factor for the surface dose rate at any time after an initial determination has been made.

The percentage of the surface dose in the central axis as a function of tissue depth is given in Figure 4. Note that the curve is a straight line when plotted on semilogarithmic paper indicating that the radiation arising from the strontium 90 applicator consists primarily of one group of beta-ray particles having a single peak energy rather than from a spectrum of beta particles made up of multiple peak energies. This curve allows one to compute the approxi-

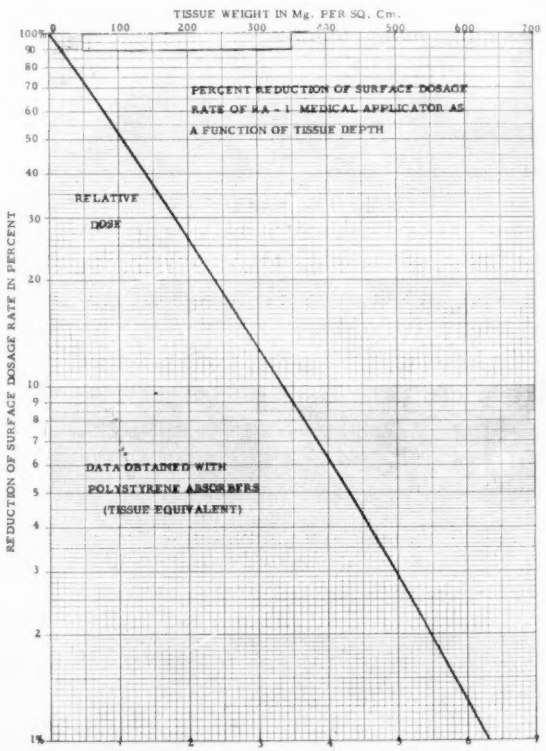

FIG. 4. This curve plotted on a semilogarithmic chart shows reduction of the surface dose in the depth. Note that at 4 mm. the dose is 6 per cent of the surface dose. The equator of the lens, the vulnerable cataract-forming zone, is about 4 mm. deep. In this series, the dosage pattern delivered about 300 rep to this depth. (Reproduced by permission from the *Tracerlab Instruction Manual.*)

mate dosage which will be present at any tissue depth directly under the central axis of the applicator.

Periodic six month calibration of the applicator may be done by means of an extrapolation ionization chamber of the type described by Failla.[1] The sole test performed by the clinician is a semimonthly routine wipe test. This consists of applying the applicator face down on a piece of filter paper and by means of a circular motion wiping the face a dozen times. The paper is then surveyed with a beta-gamma survey meter. Any significant increase over background rate indicates leakage.

The apparatus is sterilized with ST 37 antiseptic solution and 70 per cent alcohol followed by sterile water wash. Since zephiran chloride corrodes aluminum, its use is not recommended.

TECHNIQUE

The patients were jointly examined by an attending ophthalmologist (MMZ) and a radiotherapist (either BR or WL).

Surgery was performed in the following manner: After topical anesthesia and insertion of the lid speculum, the neck of the pterygium was grasped in a toothed forceps. By sharp dissection, beginning about 1 mm. in clear cornea central to the apex of the head of the pterygium, a cleavage plane was maintained as the head of the pterygium was dissected peripherally to the limbus. As soon as the limbus was transversed by the incision, the pterygium immediately retracted peripherally due to the inherent elasticity of the tissues, leaving an area of bare sclera about 4 mm. in breadth adjacent to the cornea. The pterygium was then excised. The lid speculum was removed, antibiotic ointment instilled, and a Wheeler patch applied.

Beta-ray therapy was started in the first week following surgery in the following manner: Three drops of 1 per cent pontocaine was placed into the affected eye, while the patient remained supine for three to five minutes. A gauze square was placed upon the affected eye, indicating the side to be treated. After testing for complete anesthesia, a retractor, opened as wide as comfort permitted, was adjusted. The patient was directed to focus on a marked point on the ceiling with the opposite eye to prevent motion of the eyeball.

The nurse then opened the box containing the strontium 90 applicator. The instrument, grasped by the handle, was placed directly upon the limbus of the eye so that the center of the face of the strontium 90 applicator was in direct contact with the eye at the point of surgical severance of the head of the pterygium.

The time of application was by stopwatch accuracy. At the expiration of approximately sixty seconds, the nurse said "off" and the applicator was immediately removed, wiped on a gauze dipped in antiseptic solution, and placed back in its metallic box. In this manner a dose of about 2,500 rep was delivered. This dose was repeated in fourteen days.

Antibiotic ointment was applied and a pressure bandage was placed upon the eye to be kept for two hours until anesthesia wore off.

Some useful cautionary measures in the treatment program may be stressed: (1) Do not apply the applicator before anesthesia is complete; (2) the patient must be instructed not to move the eyes during treatment; (3) the applicator must be in direct contact with the eye; and (4) the dressing, following the procedure, is essential, lest a foreign body inadvertently get into the eye without the patient's knowledge.

RESULTS

Since November 1952, a total of 256 patients with pterygia were observed. Most treatments were given with the strontium 90 applicator soon after its acquisition in 1953, although some experience was gained with radon tubes which were employed initially. A trial study in which 12 patients received beta irradiation without surgery, the dose varying from 7,500–10,000 rep given at weekly intervals, demonstrated

TABLE I

GENERAL STATISTICS—256 CASES

Age:	Maximum	85 years
	Minimum	17 years
	Average	31 years
Sex:	Male	179
	Female	77
Side:	Bilateral	51
	Unilateral	205
Site:	Nasal	231
	Temporal	25
Race:	Puerto Rican	223
	Caucasian	12
	Negro	12
	Chinese	9

the inability of beta radiation alone to control pterygia.

Of the series of 250 cases, only 166 were considered satisfactory for inclusion in the analytic study. The criterion used in determining whether a case be included was that the patient be observed for a six month period following irradiation. Patients excluded were those lost to follow-up within six months and those whose treatment was completed within the last six month period. A failure, if it appeared within a six month period, was nevertheless included.

Table I gives a statistical compilation relative to age, sex, eye involved, medial versus lateral aspect of the eye, and racial background. Several features are of special interest: the high incidence in Puerto Ricans; the absence of pterygia before early adulthood; a relatively higher incidence of nasal versus temporal involvement; and predominance of unilateral involvement.

TABLE II

PREVIOUS OPERATIONS

No. of Patients	No of Operations
7	1
10	2
8	3
3	5
1	7
Total 30 (12 per cent of all cases)	

TABLE III

BETA-RAY TREATMENTS AFTER SURGICAL EXCISION

No. of Patients	No. of Beta-Ray Treatments per Patient
18	1
122	2
16	3
14	4
56	Other treatments*
256	

* Other treatments are difficult to categorize because of multiple field applications.

Table II shows the number of patients who had had surgery prior to the specific operation in conjunction with beta-ray therapy. This group comprised 12 per cent of the patients.

Table III lists the number of treatments given to the eye after surgical excision of the pterygium. Note that most lesions were irradiated only twice at intervals of two weeks. One treatment with strontium 90 is defined as the delivery of approximately 2,500 rep surface dose. One treatment with the radon plaque is defined as a 10-minute application.

Table IV indicates the results of treatment of patients observed after six months. Of the 166 patients who were adequately followed, 6 developed recurrent pterygia. This recurrence rate of 3.6 per cent represents the best results reported to date. It stands in marked contrast to a recurrence rate of 30 per cent after surgery alone.[5] An analysis of the individual features in each of these cases is illuminating. In one patient surgery was judged to be inadequate but irradiation was attempted nonetheless to

TABLE IV

RESULTS (166 CASES)

Arrests	160 (96.4%)
Failures	6 (3.6%)

determine whether this treatment could supplement surgery. In spite of 3 doses of 2,500 rep at two week intervals, failure was evident, and recurrence appeared. In a second case, delayed beta-ray therapy was instituted three weeks following surgery. In spite of 3 doses, 2,500 rep (surface) at two week intervals, the pterygium recurred. It is conceivable that too long a period between surgery and irradiation increases the likelihood of recurrence. The third patient with recurrent disease received a single dose of 1,000 rep. This low dose was inadvertently given. Also, the patient failed to report at the two week interval. Subsequent observation in three months revealed a recurrent pterygium. Three cases with adequate surgery subjected at once to adequate irradiation showed recurrence after three, five, and six months respectively. In each of these patients a second intensive course of irradiation was ineffectual and surgery was again performed.

There were 17 cases which, despite previous surgical excisions, were cured with this specific technique of excision followed at once by beta-ray therapy.

RADIATION REACTIONS

There were immediate and delayed reactions.

The immediate reactions represented a typical syndrome of localized, nonspecific inflammation. The patients complained of photophobia, itching, and burning. Objectively, conjunctival injection, punctate keratitis, and lacrimation were noted. These reactions were self-limited, and usually of short duration, although they occasionally persisted for several weeks.

To date, the following delayed reactions were observed: (1) Telangiectasia of the conjunctiva appeared in approximately 50 per cent of the patients. It occasionally occurred as early as two years after beta-ray therapy. This observation differs from that of Merriam,[6] who stated that telangiectasia begins approximately five years after completion of therapy. There were no symptoms associated with this development; (2) keratinization of the conjunctival epithelium demonstrated by corneal scrapings appeared in one patient in the fourth year. It has persisted to date; (3) corneal vascularization and corneal scarring was not infrequent. These findings are noted after surgery alone; (4) superficial punctate keratitis was commonly seen during beta-ray therapy, and this frequently persisted for several weeks after the completion of therapy.

Although the following late radiation effects have been reported by others, none were observed in this series: (1) radiation cataract; (2) atrophy of the sclera; (3) atrophy of the ciliary body with hypotony; (4) iritis with secondary glaucoma; (5) occlusion of the angle with secondary glaucoma; (6) atrophy of the iris; (7) ulceration and perforation of the cornea with loss of the eye; (8) necrosis and perforation of the cornea with loss of the eye; (9) telangiectasis of the retina with or without vitreous hemorrhage; and (10) rhabdomyosarcomatous change in the extra-ocular musculature.

These late sequelae have either been reported in patients receiving roentgen or gamma radiation, or receiving beta-ray radiation of the order of 25,000–30,000 rep.

Cellular scrapings of the conjunctiva were studied microscopically. These findings are now being evaluated and will be the subject of a separate report.

CATARACTOGENESIS

The appearance of cataract as a late sequela of beta-ray therapy has been reported. Merriam[6] described 8 cases following beta radiation with doses ranging from 2,300–22,000 rep on the surface. The strontium 90 applicator may have a distinct advantage in this respect. Assuming that the distance from the limbus, the site where the applicator is placed, to the equator of the lens is 4 mm., the dose delivered to the lens is only 6 per cent of the surface dose (Fig. 4). The majority of eyes in this series that were treated with a surface dose

of 5,000 rep, therefore, received only about 300 rep at the equator, which is the vulnerable cataract-forming zone. Although this dose may prove to be cataractogenic, this has not yet been noted in a five year follow-up period. Obviously, future evaluation must be awaited.

CONCLUSION

Treatment of pterygia by surgery followed within one week by a beta-ray surface dose of 2,500 rep to the limbus, repeated in two weeks, is an effective procedure.

Of the 6 failures, 3 could not be adequately explained. In the other 3 cases, recurrence resulted either because of inadequate surgery, inadequate irradiation, or delay between surgery and irradiation. It becomes, therefore, evident that no amount of irradiation is a satisfactory substitute for inadequate surgery, and that if beta irradiation is given in insufficient amounts, or delayed too long after the surgery, the chances of recurrence are increased.

It is recommended that re-operation followed by beta irradiation be used routinely in the treatment of recurrent pterygia after surgery. Such a positive stand cannot be taken in the untreated case, where excision alone may prove curative. However, the 6 per cent recurrence after the combined treatment is significant, when compared with a 30 per cent recurrence after surgery alone. These facts must be weighed against possible undesirable long-term radiation effects.

At the present, a dosage schedule of 1,000 rep at weekly intervals for a period of three weeks is being used to establish whether satisfactory results can be obtained, while minimizing the occurrence of immediate and late sequelae.

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REFERENCES

1. FAILLA, G. Measurement of tissue dose in terms of same unit for all ionizing radiations. *Radiology*, 1937, *29*, 202–215.
2. FRIEDELL, H. L., THOMAS, C. I., and KROHMER, J. S. Beta-ray application to eye with description of applicator utilizing Sr^{90} and its clinical use. *A.M.A. Am. J. Ophth.*, 1950, *33*, 525–535.
3. ILIFF, C. E. Beta irradiation in ophthalmology. *Arch. Ophth.*. 1947, *38*, 415–441.
4. KAPLAN, I. I. Beta radiation therapy in ophthalmology. *Mississippi Valley M. J.*, 1948, *70*, 236–238.
5. KING, J. A., JR. Pterygium: Brief review and evaluation of certain methods of treatment. *A.M.A. Arch. Ophth.*, 1950, *44*, 854–869.
6. MERRIAM, G. R., JR. Late effects of beta radiation on eye. *A.M.A. Arch. Ophth.*, 1955, *53*, 708–717.
7. Tracerlab brochure pertaining to usage of RA-1A medical applicator. Tracerlab Inc., Boston, Mass., 1953.
8. WILSON, F. M. Applicators for beta irradiation of eye; review and comparison. *Am. J. Ophth.*, 1952, *35*, 645–656.

VOL. 81, NO. 1

RADIOACTIVE CHROMIUM 51 GAMMA RAY SOURCES*

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RADIOACTIVE chromium 51 is one of about a dozen among more than 800 artificial radioisotopes with properties which make them attractive as sources of gamma rays that are potentially useful in radiation chemotherapy. Suitable forms containing radiocobalt 60[14,15] and radiogold 198[16,17] have initially been studied previously in this laboratory.

The desirable physical properties of radiochromium 51 first drew out attention to it a dozen years ago, and attempts have been made from time to time since then to produce it in sufficient strengths and in forms suitable for use in treatment. A preliminary account of these endeavors[18] disclosed that nuclear reactor facilities had recently come into operation at the Oak Ridge National Laboratory in which chromium 51 was generated in pure chromium crystals,[18] with a specific activity that would be adequate for some purposes, provided the chromium became available in more convenient forms. Since then very pure chromium wires have been supplied to us in several diameters, and it is our purpose here to describe experiences with gamma ray sources that may interest radiotherapists.

PHYSICAL PROPERTIES OF RADIOACTIVE CHROMIUM 51

Discovery. Chromium 51 is an artificial radioisotope with atomic number 24 and atomic mass 51, the difference being due to 27 neutrons. It was discovered in 1940 by Walke, Thompson and Holt,[22] first in a titanium target that had been bombarded in a cyclotron with 16 mev. α particles, and then in a chromium target bombarded with 8 mev. deuterons. These investigators also produced it by exposing chromium to slow neutrons.

Neutron Cross Section and Specific Gamma Ray Emission Constant. Chromium 51 is now commonly generated by the nuclear reaction

$$_{24}Cr^{50}(4.3\%) \xrightarrow{n,\gamma} {}_{24}Cr^{51}$$

the thermal neutron cross section of which is 16 barns.[6] This cross section is comparable to 20 barns in the production of cobalt 60 but it is much less than the 98 barns involved in the generation of gold 198. However, the Cr^{50} target nucleus makes up only 4.3 per cent of elemental chromium, whereas cobalt 60 and gold 198 each consist of a single isotope to comprise the entire target. These considerations, coupled with the fact that the 323 kev. gamma ray is emitted in only 9.8 per cent of the disintegrations of Cr^{51} (Fig. 1), account for the principal difficulties encountered in making chromium 51 gamma-ray sources with sufficient activities, in contrast to the ease with which cobalt 60 and gold 198 sources could be obtained in our earlier studies.

Calculations based on these factors reveal that about 650 mc will be present in a gram of chromium at the end of two weeks in a thermal neutron flux of 10^{13} n/cm.^{2}/sec. Further calculations show that, chiefly because there is only one gamma ray emitted in each ten disintegrations, the gamma ray flux will be only about 0.17 r per hour at 1 cm. from a 1 mc source. Thus, useful strengths have not been obtainable until recently.

Decay Scheme. Chromium 51 decays by electron capture to stable vanadium 51 according to the decay scheme proposed by Bunker and Starner,[2] a modification of

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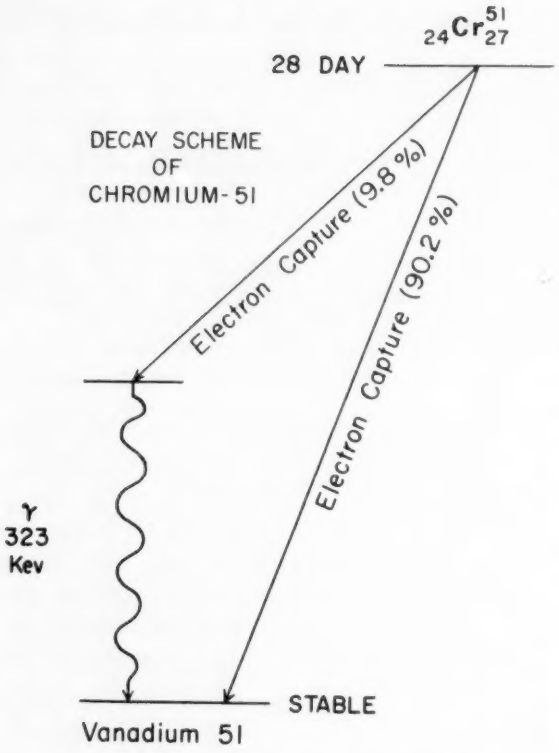

FIG. 1. Decay scheme of radioactive chromium 51. Modified from that proposed by Bunker and Starner.[2]

which is shown in Figure 1. *The 323 kev. gamma ray emitted in approximately 10 per cent of the disintegrations is the feature that makes chromium 51 attractive.* Especially significant also is the fact that *no* undesirable and useless *beta particles are emitted.* The very soft x ray, characteristic of vanadium, that follows electron capture in each disintegration has an energy of less than 5 kev., and therefore it will be almost completely selfabsorbed in the metallic sources. The comparatively few of these weak x rays, which do escape from the surface, will have an estimated half-thickness in water of less than 0.02 cm., based on Victoreen's calculated values of mass absorption coefficients.[21] Hence, they can be considered as being inconsequential for interstitial applications. Similarly, the soft conversion electrons occurring in only 0.15 per cent of the disintegrations need be of no concern.

Gamma Ray Absorption. Interpolations of Fano's[5] values for mass absorption coefficients for "narrow-beam" attenuation of photons in water and in lead give the values in Table 1 for the gamma rays emitted by chromium 51, gold 198, and cobalt 60.

The half-thickness values were calculated from the familiar relationship,

$$\text{half-value layer} = 0.693/\mu_m \cdot \rho$$

where μ_m is the mass absorption coefficient and the density, ρ, is taken as 1.00 for water and 11.3 for lead.

Decay Rate. The discoverers of chromium 51 found that it decayed with a half-life of 26.5 ± 1.0 days.[22] Lyon[13] reported a half-life of 27.75 ± 0.3 days. Kafalas and Irvine[12] found it to be 27.9 ± 0.2 days. A half-life of 28 days was obtained in this laboratory (Fig. 2) for a radioactive chromium cylinder, the decay of which was followed for more than eight half-lives by means of a Lauritsen quartz-fiber electroscope. In Table II are listed the percentages of the initial activity remaining, and the reciprocals, as a function of time, for a

TABLE I

GAMMA-RAY ABSORPTION IN WATER AND IN LEAD

	Cr^{51}	Au^{198}	Co^{60}
Gamma-Ray Energy (mev.)	0.323	0.412	1.25 (Mean)
Mass Absorption Coefficient, μ_m, for Water (cm.^{2}/gm.)	0.115	0.104	0.0632
Half-Thickness in Water (cm.)	6.03	6.66	11.0
Mass Absorption Coefficient, μ_m, for Lead (cm.^{2}/gm.)	0.330	0.218	0.060
Half-Thickness in Lead (cm.)	0.186	0.281	1.02

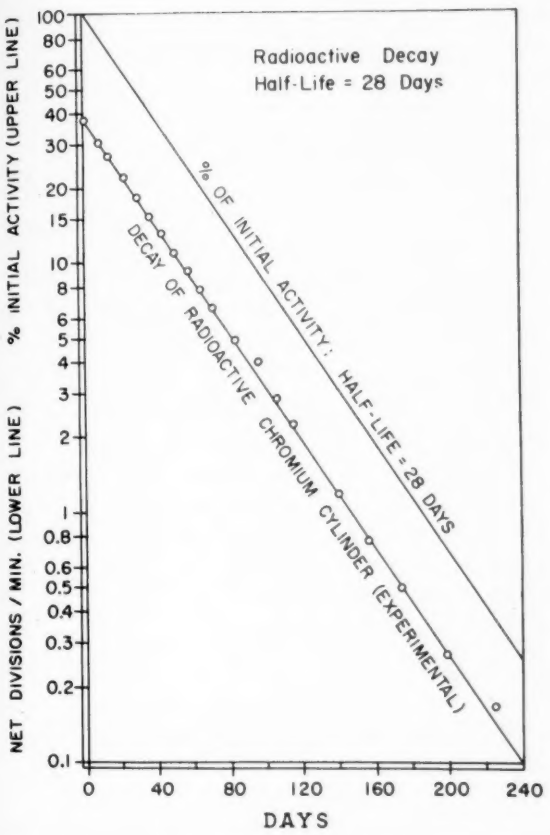

FIG. 2. *Upper Line.* Percentage of initial activity remaining as a function of time for a radioisotope that decays with half-life of 28 days. *Lower Line.* Decay of a radioactive chromium cylinder determined experimentally over more than eight half-lives by means of a Lauritsen quartz-fiber electroscope.

radioisotope that decays with a half-life of 28 days.

SOURCES OF CHROMIUM 51

The last few lots of chromium sent to the Oak Ridge National Laboratory for radioactivation have been in the form of cylinders 2.5 mm. long and 0.8 mm. in diameter. They were cut from 0.031 inch chromium wire by means of a holding template and a high-speed cutting wheel, 0.010 of an inch thick. After inspection under a low-power lens and removal of any burrs with a small hand stone, the cylinders were tested for ease of manipulation in the implantation gun described by Hodt, Sinclair and Smithers.[10] They were then selected with the aid of a torsion balance into lots with variation less than ± 1 per cent from the mean weight of about 8.5 mg. Several of the cylinders are shown in Figure 3.

STRENGTHS OF SOURCES

For Permanent Implantations. After two weeks in a thermal neutron flux of 2×10^{13} n/cm.^{2}/sec., each of the cylinders was found to have a gamma ray activity of 2.5 r/hr. at 1 cm. (rhcm.) initially when compared by means of a Lauritsen quartz-fiber electroscope to the same radium standard and in the manner described previously.[17] The roentgens-total-at-1-cm. (rtcm.) during complete decay of one of these cylinders would therefore be $2.5\times28\times24/0.693 = 2{,}400$ rtcm. At the end of the first half-life, then, the remaining 1,200 rtcm. will still be a strength that would be satisfactory to many radiotherapists who might choose to implant radioactive chromium cylinders permanently.[3]

Studies in rats have indicated that these cylinders appear to be as inert chemically as were the radioactive chromium crystals described previously.[18] Radioactive chrom-

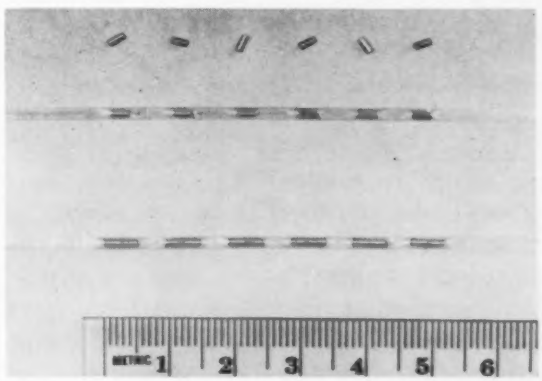

FIG. 3. *Upper.* Six cylinders 0.8×2.5 mm. cut from 0.031 inch pure chromium wire. *Middle.* Cylinders incorporated into a nylon ribbon and held in place by the resiliency of the ribbon, as suggested by Henschke and his co-workers.[9] *Lower.* Two of the chromium cylinders were placed in each "cell" spaced 1 cm. apart in the nylon ribbon. The radioactivity of each cell may be varied readily by inserting cylinders of equal strength received in a given lot, or by choosing each cylinder in the pair from lots received at different times.

TABLE II

PERCENTAGES AND RECIPROCALS OF THE INITIAL ACTIVITY REMAINING AFTER VARIOUS TIMES, CALCULATED FOR A RADIOISOTOPE WITH HALF-LIFE

$t_{1/2} = 28$ *days*

Per cent remaining at time, t (days) = antilog $(2.00000 - 0.01075\ t)$

Time Days	Per Cent Remaining	Reciprocal	Time		Per Cent Remaining	Reciprocal
			Days	Weeks		
0	100.0	1.000	35	5	42.0	2.38
1	97.6	1.025	42	6	35.4	2.83
2	95.2	1.051	49	7	29.7	3.36
3	92.8	1.077	56	8	25.0	4.00
4	90.6	1.104				
5	88.4	1.132	63	9	21.0	4.76
6	86.2	1.160	70	10	17.7	5.66
7	84.1	1.189	77	11	14.9	6.73
8	82.0	1.219	84	12	12.50	8.00
9	80.0	1.250				
10	78.1	1.281	91	13	10.51	9.51
11	76.2	1.313	98	14	8.84	11.31
12	74.3	1.346	105	15	7.43	13.45
13	72.5	1.380	112	16	6.25	16.00
14	70.7	1.414				
15	69.0	1.450	119	17	5.26	19.0
16	67.3	1.486	126	18	4.42	22.6
17	65.6	1.523	133	19	3.72	26.9
18	64.0	1.561	140	20	3.13	32.0
19	62.5	1.600				
20	61.0	1.641	168	24	1.562	—
21	59.5	1.682	196	28	0.781	—
22	58.0	1.724	224	32	0.391	—
23	56.5	1.767	252	36	0.195	—
24	55.2	1.811				
25	53.8	1.857	280	40	0.098	—
26	52.5	1.903	308	44	0.049	—
27	51.3	1.950	336	48	0.024	—
28	50.0	2.000	364	52	0.012	—

ium cylinders that were removed 18 months after implantation intramuscularly had retained the original shiny appearance and the periacicular tissues showed no gross evidence of chemical injury.

Removable Sources. One milligram of radium enclosed in 0.5 mm. of platinum has a gamma-ray output of 8.25 rhcm.[19] Therefore the initial flux-rate of each of the 0.8 $\times$2.5 mm. cylinders is the equivalent of $2.5/8.25 = 0.30$ mg. of radium in the filter that is commonly used to remove some of the β particles emitted by radium.

For the fabrication of removable gamma-ray sources, each cylinder should have an activity a few times greater than this. Should cylinders 0.5 cm. long cut from a chromium wire with a diameter of 1.2 mm. be radioactivated for 4 weeks (one half-life) in the maximum thermal neutron flux of 2×10^{13} n/cm.^{2}/sec. that is presently available for medical purposes, they would have an initial gamma-ray output of approximately 20 rhcm., equivalent to about 2.4 mg. of radium.

When neutron fluxes of the order of 10^{14} n/cm.^{2}/sec. become generally available in the near future,[1] it will be feasible to generate sufficient activity in our present 0.8 $\times$2.5 mm. chromium cylinders to fill all

needs of a radiotherapist for gamma-ray sources for interstitial and similar uses. The strengths in these small cylinders will then be adequate for loading removable sources such as plastic threads[8,9,11] or steel needles, and for incorporation into molds or plaques when they are first received at 4-weekly (*i.e.*, one half-life) intervals. Combinations of the cylinders from the most recent shipment with those of former lots (lower thread in Figure 3), will permit loadings to any strength as well as to differential strengths for any purpose.

Then the cylinders, which have decayed to the point that they are no longer sufficiently active for reloading the removable sources of gamma rays, will become available for permanent implantations by means of trocar or "gun" during a period of a month or two. Finally, the cylinders that have become too weak for any purpose can be set aside for the radioactivity to die out (Table II) before reactivation in the reactor.

DISCUSSION

The recent analysis by Hale[7] demonstrated that correction factors "for the differences in the absorption and scattering in tissue of the gamma rays of radium compared with the other [γ-isotopes useful in interstitial therapy] is less than 10 per cent for gamma-ray energies of 0.25 to 2.0 mev., and for distances within 5 cm. of the source." Obviously, since the 0.323 mev. gamma ray emitted by chromium 51 falls well within this range of energies, there need be no hesitancy in adapting the familiar dose-rate tables for radium in applying chromium 51 in removable sources, provided the radiotherapist adjusts the strength of his sources to correspond in terms of roentgens-per-hour-at-1-cm. (rhcm.) and he bears in mind that the radioactive chromium sources will decay to 84 per cent of the original activity during one week.

Cohen[3] compared several properties of seven artificial gamma isotopes with radon; *i. e.* Au^{198}, $t_{\frac{1}{2}}=2.69$ days; Rn^{222}, $t_{\frac{1}{2}}=3.83$ days; Bi^{206}, $t_{\frac{1}{2}}=6.40$ days; I^{131}, $t_{\frac{1}{2}}=8.0$ days; Ba^{140}, $t_{\frac{1}{2}}=12.8$ days; Cr^{51}, $t_{\frac{1}{2}}=26.5$ days; Ir^{192}, $t_{\frac{1}{2}}=74$ days and Ta^{182}, $t_{\frac{1}{2}}=111$ days. He concluded that "The longer-lived materials are shown to have certain advantages, and it is suggested that moderately long-lived sources with half-lives of the order of 20 days are likely to prove superior to conventionally used materials."

The 28 day half-life of chromium 51 exceeds the suggested 20 day half-life by 40 per cent. Certainly it should be more suitable than the tantalum 182 with a half-life four times as long that was used for permanent implantations[4] and iridium 192 with a half-life of 74 days which Cohen states is excessively long-lived also.[3]

On the other side of 20 days, the 12.8 day half-life of the Ba^{140} in his list falls short by about the same interval, viz., by 36 per cent. Also Ba^{140} gives rise to radioactive lanthanum 140, which is reported to have a half-life of 40 hours, so that attempts to use this mother-daughter combination would frequently be complicated by considerations of delays for equilibrium to become established. The combination gives rise to a dozen gamma rays of widely different energies, four of which are less than 0.165 mev., so that difficulties in the use of it would be expected to arise because of uncertainties of dosimetry. Moreover, the emission of several hard β particles with energies up to 2.26 mev. would require absorbers that would be distinctly disadvantageous in comparison with *chromium 51* which *emits no beta particles* and therefore requires no absorber shield. Then, too, barium falls next above radium in the same family in the periodic table of the elements so that the chemistry of the two is similar and the same problems of encapsulation of a radioactive powder would arise.

In addition to the artificial gamma isotopes considered by Cohen,[3] there is rubidium 86 with a half-life of 19.5 days. It emits a single 1.08 mev. gamma ray in about 9 per cent of its disintegrations; but it, too, emits very energetic β particles that would require removal by screens. Also, it

falls between potassium and cesium in the periodic table and therefore it should be so strongly electropositive as to raise again the same problem of encapsulation of a radioactive powder.

In this respect the chemical inertness and the mechanical features of the radioactive chromium cylinders, coupled to the suitability of the physics of Cr^{51} for the purpose, make them appear to be particularly attractive. Hale's[7] observation that increased scatter largely compensates for the greater absorption of gamma rays in the lower part of the 0.25–2.0 mev. energy range is interpreted to mean that the 0.323 mev. gamma ray of Cr^{51} is especially advantageous because of the ease of protection of personnel. The calculated "narrow-beam" half-thickness in lead of less than 2 mm. greatly simplifies problems of shielding, not only in transit, but in the preparation and insertion of gamma ray sources as well.

Further, as regards protection, a special advantage to the operators is the favorable factor of the 28 day half-life which requires that the sources will have much lower initial activities when they are being inserted for complete die out in permanent implantations. Thus exposures to personnel during the implantations, in comparison with those involved when Au^{198} or Rn^{222} are used will be greatly reduced.

For special purposes there would be the opportunity to design applicators with slots in one side of the thinned parts of "directional" platinum partial filters, even hollow needles about 2.0–2.5 mm. in diameter which are eccentric in cross section. These could be fixed in place in a manner which would provide well over one half-thickness of protection to the healthy tissues opposite the more active "slot" aimed at the area being treated.

Similarly, advantage might be taken of the ready absorbability of the 323 kev. photon in lead, tantalum, gold or platinum to form "directional" applicators with built-in screening to achieve special dose distributions for some purposes. It will be recalled that Neary[20] incorporated radium into massive platinum screens for insertion into the vagina and thereby greatly diminished exposures to the rectum and other mid-line structures while obtaining doses of 5,000 r at the pelvic wall during 72 hours, through the ports in his uterovaginal miniature radium bomb. Near the conclusion of his paper he states " . . . But there is a yet more promising possibility for the future. Professor Mayneord has pointed out that supplies of radio-elements may become available giving powerful and concentrated sources of X radiation of various qualities. With such a source of, say, 400-kV radiation, the application of the screening principle would be tremendously simplified—millimetres of lead would suffice where before centimetres of platinum were used. The great saving of space so gained would permit the design of more complex multi-source intracavitary units of greater efficiency, and applicable to practically any case. . . . "

It is estimated that a chromium cylinder only 1 cm. long cut from a wire supplied to us that has a diameter of 1.5 mm. would have a gamma ray flux-rate well in excess of 100 r per hour at 5 cm., after the cylinder is radioactivated a few weeks in a neutron flux of about 10^{15} n/cm.^{2}/sec. A centimeter of lead or tantalum, or about half this thickness of gold or platinum, would absorb all but a few per cent of the 323 kev. gamma rays. Thus, it would be very simple to incorporate radioactive chromium cylinders into the very effective differential screening applicators that Neary predicted as a " . . . promising possibility for the future. . . . "

SUMMARY

1. Radioactive chromium 51 is advocated as a gamma isotope that should be eminently suitable for interstitial and other applications in radiation therapy. Presently, it is being generated in cylinders 2.5 mm. long and of 0.8 mm. diameter that are cut from pure chromium wire.

2. The cylinders emit 323 kev. gamma

rays and decay with a half-life of 28 days. Because *they emit no β particles* and the soft x rays emitted incidental to electron capture are almost completely absorbed within the cylinders, they may be considered to be purely monoenergetic gamma-ray sources.

3. The radioactive cylinders are very inert chemically and they have ideal mechanical properties.

4. Neutron fluxes presently available generate specific activities in the cylinders that are adequate for permanent implantations by conventional methods or by means of an implantation gun.

In the fluxes soon to become available for medical purposes, cylinders with the above dimensions can be made sufficiently radioactive to fill all needs of a radiotherapist for interstitial gamma-ray sources. When first received, they can be incorporated into removable plastic threads and metal needles, as well as into molds or plaques. After the activities have decayed during repeated usage in this manner to the point that they are no longer adequate for removable sources, the cylinders will be recoverable for use in permanent implantations.

5. Radioactive chromium 51 generated in larger chromium cylinders during a few weeks in the thermal neutron fluxes of 10^{15} n/cm.^{2}/sec., now known to exist, will constitute sources that can be incorporated conveniently into "directional" applicators for insertion into body cavities. It will be simple to design these to protect normal tissues not aligned with the radiation ports in the absorber screen that are directed toward the volume under treatment.

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REFERENCES

1. Aebersold, P. C. Personal communication. March 15, 1958.
2. Bunker, M. E., and Starner, J. W. Decay of Ti^{51} and Cr^{51}. *Phys. Rev.*, 1955, *97*, 1272–1275.
3. Cohen, L. Selection of gamma-ray emitting isotopes as permanent implants in treatment of cancer. *Physics in Med. & Biol.*, 1958, *2*, 229–233.
4. Cohen, L. Protracted interstitial irradiation of tumours using ^{182}Ta. *Brit. J. Radiol.*, 1955, *28*, 338–340.
5. Fano, U. Gamma-ray attenuation. *Nucleonics*, 1953, *11*, No. 8, 8–12.
6. Friedlander, G., and Kennedy, J. W. Nuclear and Radiochemistry. Appendix C. John Wiley & Sons, Inc., New York, 1955.
7. Hale, J. The use of interstitial radium dose rate tables for other radioactive isotopes. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1958, *79*, 49–53.
8. Henschke, U. K., James, A. G., and Myers, W. G. Radiogold seeds in clinical radiation therapy. *Radiology*, 1954, *63*, 390–399.
9. Henschke, U. K., James, A. G., and Myers, W. G. Radiogold seeds for cancer therapy. *Nucleonics*, 1953, *11*, No. 5, 46–48.
10. Hodt, H. J., Sinclair, W. K., and Smithers, D. W. A gun for interstitial implantation of radioactive gold grains. *Brit. J. Radiol.*, 1952, *25*, 419–421.
11. James, A. G., Henschke, U. K., and Myers, W. G. The clinical use of radioactive gold (Au^{198}) seeds. *Cancer*, 1953, *6*, 1034–1039.
12. Kafales, P., and Irvine, J. W., Jr. Nuclear excitation functions and thick target yields: (Cr+d). *Phys. Rev.*, 1956, *104*, 703–705.
13. Lyon, W. S. Disintegration of Cr^{51}. *Phys. Rev.*, 1952, *87*, 1126.

14. MYERS, W. G. Radioactive needles containing cobalt 60. *Science*, 1948, *107*, 621.
15. MYERS, W. G. Applications of artificially radioactive isotopes in therapy. I. Cobalt^{60}. AM. J. ROENTGENOL. & RAD. THERAPY, 1948, *60*, 816–823.
16. MYERS, W. G., and COLMERY, B. H., JR. Radioactive Au^{198} in gold seeds for cancer therapy. *Cancer Res.*, 1952, *12*, 285–286.
17. MYERS, W. G., COLMERY, B. H., JR., and MCLELLON, W. M. Radioactive gold-198 for gamma radiation therapy. AM. J. ROENTGENOL., RAD. THERAPY & NUCLEAR MED., 1953, *70*, 258–273.
18. MYERS, W. G. Neutron-radioactivated pure chromium crystals as sources of gamma rays for radiation chemotherapy. *Radiology*, 1956, *66*, 268.
19. Modification of the basis for roentgen calibrations between 0.5 and 3 Mev. National Bureau of Standards Technical News Bulletin, Dec., 1957, *41*, 198.
20. NEARY, G. J. Physical aspects of intracavitary radium treatment of carcinoma of cervix uteri. Part III. A new applicator. *Brit. J. Radiol.*, 1947, *20*, 454–469.
21. VICTOREEN, J. A. Roentgen rays: Measurement of quality. In: Medical Physics. Vol. II. Year Book Publishers, Inc., Chicago, 1950, pp. 887–894.
22. WALKE, H., THOMPSON, F. C., and HOLT, J. K-electron capture and internal conversion of Cr^{51}. *Phys. Rev.*, 1940, *57*, 171–176.

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STUDY OF THE HEMORRHAGIC DIATHESIS IN A PATIENT FOLLOWING INTRAPERITONEAL INSTILLATION OF RADIOCHLORIDE 38*

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INFORMATION about the hemorrhagic disorder which follows overexposure of humans to ionizing radiation has been obtained essentially from the meager observations of the atom bomb casualties in Hiroshima and Nagasaki[11] and observations of accidentally overexposed persons.[8,9,10,14] Available data consist of the clinical course, estimated exposure dose, platelet counts, blood clotting times, prothrombin times, and marrow counts.

This report is of the hemorrhagic diathesis in a patient who had radiochloride instilled into the peritoneal cavity for peritoneal carcinomatosis secondary to ovarian cystadenocarcinoma. The bleeding tendency which followed this form of radiation therapy was similar to that described in animals irradiated with ionizing rays.

REPORT OF A CASE

A thirty-five year old female had a radical mastectomy sixteen months before admission for carcinoma of the right breast. No tumor was found in the axillary lymph nodes nor were any metastases demonstrable by roentgenologic or clinical examination.

Eleven months before admission a bilateral oophorectomy and left salpingectomy were performed for papillary cystadenocarcinoma of the left ovary. A tumor mass was removed from around the descending colon and several peritoneal implants were biopsied. The excised tumor did not resemble the carcinoma of the breast removed previously.

Nine months before admission the patient developed ascites. The ascitic fluid contained undifferentiated cells, the origin of which it was not possible to determine. Thereupon, seven doses of radiochloride 38 (864 millicuries each) were injected into the peritoneal cavity over twenty-four days.* Chloride 38 has a half life of 38.5 minutes and is an effective gamma ray emitter. Ascites subsided until two months before admission but then recurred. Radiochloride was administered again—4 doses of 1.2 curies each—in twenty-three days. The development of large bowel obstruction by a tumor, probably a recurrence of the incompletely excised ovarian tumor which invaded bowel wall at the previous operation, caused the termination of radiochloride therapy and required a cecostomy for decompression. Three days later at laparotomy the tumor was found to be irresectable, and a permanent colostomy was performed.

Approximately eighteen days after the last dose of radiochloride, the patient noted "bruises" on her legs. The number of purpuric areas increased and in five days became confluent and appeared on the arms and trunk as well. Blood clotting studies were started when the petechiae first appeared.

The hemograms were normal sixteen and eleven months before the final admission. About two weeks after the last course of radiation therapy, the hemoglobin was 12.5 gm., red blood cell count 3,800,000, white blood cell count 3,800, with 66 per cent granulocytes and 34 per cent lymphocytes. The patient did not receive blood transfusion during the preceding eleven months.

The purpura reached its greatest intensity in five days then faded gradually and disappeared completely in twenty days. Gross bleeding did not occur though occasional red blood cells were found in catheterized urine specimens.

The patient was weak during the terminal three months in the hospital. She developed leg edema and bilateral pleural effusion which required aspiration twice while she had purpura and thrice thereafter. She received one-half liter

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bank blood transfusions twice during the purpuric phase and twice later for anemia (Hb 9.5). Her appetite remained good until two weeks before death. Her temperature remained 99° F. with occasional elevations to 100° or 101° F. Loss of hair or oropharyngeal ulceration never occurred.

INVESTIGATION OF THE CLOTTING DEFECT

Bleeding time was determined on the forearm by Ivy's method[15] with the sphigmomanometer cuff inflated to 40 mm. Capillary fragility was determined according to Rumple-Leeds.[15] The petechiae in a 5 cm. circle on the antebrachium were counted after ten minutes. Clotting time was determined according to Lee-White[15] at 37° C. in 11 mm. diameter Pyrex tubes. Clot retraction was observed after one hour and twenty-four hours. The volume of extruded serum was expressed as percentage of total blood specimen volume.[15] Platelet counts were done on venous blood by the direct method.[15] The diluting fluid contained ½ per cent formaldehyde but no dye.

Plasma for prothrombin studies was separated from a mixture of 9 cc. blood drawn quickly without frothing through a No. 19 dodecyl chloride coated needle into a siliconated syringe containing 1 cc. of 3.8 per cent sodium citrate. One stage prothrombin time determinations were done on mixtures of .1 cc. plasma and .2 cc. simplastin at 37° C. Serum prothrombin times were determined according to Wintrobe[15] using purified bovine fibrinogen and simplastin. The clotting mixture consisted of .1 cc. serum and .2 cc. simplastin with .2 mg. fibrinogen.

Two stage prothrombin assays were done at 18° C. by the Sternberger method;[13] .6 cc. plasma or serum was added to a mixture of .1 cc. .2 molar calcium chloride, .3 cc. aqueous extract of acetone dried rabbit brain and 1 cc. 50 per cent ethanol. The clotting time of .2 cc. of a suitable dilution of this mixture in 25 per cent ethanol after ten minutes of incubation and .2 cc. of fibrinogen reagent was determined and converted to units from a previously constructed graph. One unit of prothrombin was defined as that which upon conversion to thrombin clotted an equal volume of fibrinogen reagent in fifteen seconds at 18° C.

Recalcified plasma clotting times were determined according to Ferguson *et al.*[7] Mixtures of 100 per cent, 50 per cent, 25 per cent, 0 per cent patient's plasma and pooled fresh normal plasma were used.

Bone marrow specimens were obtained by sternal puncture during the purpuric phase and after purpura had faded.

RESULTS

The results are presented in Table 1. The following comments are added for clarity: the value of 48 per cent-52 per cent for clot retraction is for people with a normal hematocrit. Blood retracts better when the hematocrit is low because a larger volume of serum can be expressed. As this patient had a low hematocrit, the impairment of clot retraction was even greater than a similar degree of impairment in a normal individual. Incubation of the clot for twenty-four hours at 37° C. did not show

TABLE I

Day of Observation	Purpura	Bleeding Time (min.)	Capillary Fragility	Clotting Time (min.)	Per Cent Clot Retraction		Platelet Count	Prothrombin Activity Stage		Prothrombin Residual Stage		Recalcified Plasma Clotting Time (min.)					Normal Test
					1 hr.	1 da.		1 sec.	2 units	1 sec.	2 units	100% 0	75% 25	50% 50	25% 75	0% 100	
1	+	6	34	19	10	40	42,400					1.8	1.9	2.1	2.8	3.4	
2	++	8.5	32	18	10	40	54,800	17	98	32.2	38	2	2	2.3	2.8	3.4	
5*	++++	9.5	35	21	6	30	37,600	15.1	98	32	34	1.9	2	2.2	2.9	3.8	
9	+++	10	30	19	8	30	52,400	16	95	38.1	31	1.9	2	2.2	2.6	3.6	
13	+	7.5	28	19	10	28	60,800	14.9	101	52.3	16	2	1.9	2.1	2.4	2.9	
19	±	5	28	15.5	18	23	85,200	15	100	68	7	2.1	2	2.2	2.5	2.8	
27*	−	3.5	22	14	28	54	106,000	15	99	72	5	1.8	2	2.1	2.3	2.4	
42	−	3.5	14	10	40	54	168,000	15.1	98	76	5	2	2	2	2.2	2.4	
60	−	2.5	14	10	38	56	142,000	15.2	99	78	5	2.1	2.3	2.1	2.3	2.5	

* Marrow examined.

excessive fibrinolytic activity at any time during the patient's illness.

The prothrombin activity of sera which had been clotted ninety minutes was reduced by both, one stage and two stage assays. When tested by the one stage assay, the sera from blood which had been clotted for fifteen minutes consistently showed a higher prothrombin activity than plasma. Similar findings in irradiated dogs have been reported upon.[7]

The recalcified plasma clotting times always remained within normal limits, indicating absence of anticoagulants from the patient's blood.

The bone marrow was markedly hypoplastic before as well as after purpura.

DISCUSSION

The hemorrhagic diathesis which follows overexposure of laboratory animals to ionizing radiation is characterized by thrombocytopenia and impaired prothrombin consumption. Prolonged clotting time, purpura, increased capillary fragility, increased recalcified plasma clotting time and impaired clot retraction have also been reported.[4] Thrombocytopenia, prolonged clotting time and purpura have been documented in humans also, during the hemorrhagic phase of the radiation syndrome.[6,8,11,14]

Bleeding in irradiated humans and various laboratory animals has been attributed primarily to increased capillary fragility, decreased platelets, and a circulating heparin-like anticoagulant which can be neutralized with protamine or toluidine blue.[1,2,12] The correction of bleeding or clotting time by antiheparin drugs is not a universal finding, however; neither is a circulating anticoagulant always demonstrable by the clotting time of recalcified plasma. The prolonged clotting time of blood from three humans who bled from radiation injury was correctable by the addition of toluidine blue to a sample of blood in a test tube.[10] Antiheparin drugs were not administered to the patients; their effect *in vivo* was therefore not determined.

Thrombocytopenia in the laboratory animal is a consistent finding during the hemorrhagic phase of the radiation syndrome. This bleeding can be prevented, the clotting of shed blood improved, and capillary fragility decreased by transfusion of platelets.[4,5,12] Thrombocytopenia is also prevalent in humans exposed to excessive ionizing radiation. Platelet counts as low as 10,000–12,000 have been reported.[8]

The results of the prothrombin consumption test on our patient were similar to those on laboratory animals irradiated internally[7] or externally.[2–5]

The effects of exposure to ionizing radiation cannot be compared accurately in different species or groups of the same species. Marked variability in species and individual sensitivity and inability to measure the effective radiation energy delivered make it unreliable to extrapolate animal experimentation to man or even to predict the response in an accidentally overexposed individual. Relatively small calculated doses have caused severe disease and death in some patients,[10] while larger calculated doses were not so harmful in others.[8,9]

The clinical response of patients injured by ionizing rays has been divided into four chronologic phases: the initial period of prostration and gastrointestinal symptoms; the period of relative well being; the period of toxemia with fever, hemorrhage, infection, oropharyngeal ulceration, epilation; and, the period of either recovery or death. We do not know whether patients with internal ionizing radiation injury manifest a different clinical course or whether—in our case—the peritoneal carcinomatosis and bowel obstruction obscured the usual clinical pattern.

SUMMARY

Studies upon the clotting defect in a thirty-two year old female patient who received radiochloride 38 intraperitoneally for carcinomatosis are presented. The patient developed purpura, thrombocytopenia, prolonged bleeding and clotting times, increased capillary fragility and decreased clot retraction. The bone marrow

was hypoplastic. Prothrombin utilization was diminished though plasma prothrombin activity was normal. Fibrinolytic activity was normal. Circulating anticoagulants were not demonstrable.

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REFERENCES

1. ALLEN, J. G., and JACOBSON, L. O. Hyperheparinemia: Cause of hemorrhagic syndrome associated with total body exposure to ionizing radiation. *Science*, 1957, *105*, 388–389.
2. CRONKITE, E. P. Hemorrhagic syndrome of acute ionizing radiation illness produced in goats and swine by exposure to atomic bomb at Bikini, 1946. *Blood*, 1950, *5*, 32–45.
3. CRONKITE, E. P. Atomic Medicine. Behrens, C. F., Editor. Second edition. The Williams & Wilkins Company, Baltimore, 1953, pp. 137–141.
4. CRONKITE, E. P., and BRECHER, G. Defects in Hemostasis Produced by Whole Body Irradiation. Blood Clotting and Allied Problems. Flynn, J. E., Editor. Transactions, Fifth Conference, New York, Josiah Macy, Jr. Foundation, 1952, p. 171.
5. CRONKITE, E. P., JACOBS, G. J., BRECHER, G., and DILLARD, G. Hemorrhagic phase of acute radiation syndrome due to exposure of whole body to penetrating ionizing radiation. AM. J. ROENTGENOL., RAD. THERAPY & NUCLEAR MED., 1952, *67*, 796–804.
6. DEN HOED, D., LEVIE, B., and STRAUB, M. Serious injury of blood in consequence of teleroentgenotherapy of whole body. *Acta radiol.*, 1938, *19*, 151–162.
7. FERGUSON, J. H., ANDREWS, G. A., and BRUCER, M. Blood-clotting studies on dogs internally irradiated with radio-gold. *Proc. Soc. Exper. Biol. & Med.*, 1952, *80*, 541–545.
8. GUSKOVA, A. J., and BAISOGOLAV, G. D. Two cases of acute radiation disease in man. *Proc. Internat. Conf. on Peaceful Uses of Atomic Energy, United Nations*, 1956, *11*, 35.
9. HASTERLIK, R. J., and MARINELLI, L. L. Physical dosimetric and clinical observations on four human beings involved in accidental critical assembly excursion. *Proc. Internat. Conf. on Peaceful Uses of Atomic Energy, United Nations*, 1956, *11*, 25.
10. HEMPELMANN, L. H., LISCO, H., and HOFFMAN, J. G. Acute radiation syndrome: Study of 9 cases and review of problem. Part I. *Ann. Int. Med.*, 1952, *36*, 279–510.
11. LEROY, G. V. Hematology of atomic bomb casualties. *Arch. Int. Med.*, 1950, *86*, 691–710.
12. ROSS, M. H., FURTH, J., and BIGELOW, R. R. Changes in cellular composition of lymph caused by ionizing radiations. *Blood*, 1952, *7*, 417–428.
13. STERNBERGER, L. A. Stabilization of thrombin in plasma; development of simple 2-stage method for determination of prothrombin. *Brit. J. Exper. Path.*, 1947, *28*, 168–177.
14. TSUZUKI, M. Radiation injury due to radioactive fallout. *Proc. Internat. Conf. on Peaceful Uses of Atomic Energy, United Nations*, 1956, *11*, 132.
15. WINTROBE, M. M. Clinical Hematology. Fourth edition. Lea & Febiger, Philadelphia, 1956.

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TIME-DOSE RELATIONSHIP IN STAGE I CARCINOMA OF THE UTERINE CERVIX*

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SOME seventeen years ago Margaret Tod conducted a study of time-dose relationship in the management of carcinoma of the uterine cervix by radiation therapy.[2] She expressed an interesting concept which was described as the "supralethal effect." This theory suggested that treatment failures might result from overdosage to the area of the parametrial triangle in endeavoring to raise dosage levels at the lateral pelvic wall.

Although an attempt to achieve uniformity of dosage distribution throughout a tumor mass and its possible routes of lymphatic extension has been the goal of most radiation treatment techniques, the situation in carcinoma of the cervix has been somewhat unique. Here the accessibility of the uterine and vaginal cavities has allowed for the placement of radiation sources which can contribute intense doses to the areas at risk. When combined with radiation from external sources, dosage levels have been raised to theoretically effective levels for many years. Thus the problems of "too much" radiation as well as "too little" radiation have naturally evolved during our clinical experience.

The present report is the result of clinical observations along this line in an attempt to define a range of optimal dosage. A few years ago a study of early results in the treatment of carcinoma of the cervix uteri with a combination of external radiation from the cobalt 60 apparatus and intracavitary radium was made.[1] This indicated that the doses that had been delivered were low, which was a result of conservatism in the application of a new modality for the primary treatment of private patients. It was suggested that these dosage levels could be raised safely without increasing complications. This was done arbitrarily and we now have a small series of patients so treated to compare with the earlier ones. Because of the fact that any effect of overdosage should become manifest in the management of early and presumably curable tumors, the clinical Stage I cases were selected for study. Of course such a report presents many disadvantages. The number of patients is small, the follow-up time during which they have been at risk is short, and the difference in dosage range to which the patients have been treated has not been great. Despite these obvious objections, it is necessary to make such an analysis of early results in order to give direction for future changes in treatment techniques.

Although a kilocurie cobalt 60 teletherapy apparatus has been available at the Los Angeles Tumor Institute since April, 1952, it was at first used to treat only patients with advanced primary or recurrent tumors in the management of carcinoma of the uterine cervix. Late in 1953, patients with early primary lesions were included. Between January 1, 1954, and December 31, 1955, 26 patients with primary Stage I lesions were treated. The usual plan was to deliver 2,000 r tumor dose to the midpelvis through two anterior and two posterior 10×15 cm. portals, followed by radium application with a combination of intrauterine tandem and intravaginal cylinders in two sessions two weeks apart. Each of these sessions would involve an exposure of 2,500 to 3,000 milligram hours with a calculated tumor dose of 2,230 to 2,430 r to Point "A" and 670 to 730 r to Point "B." Thus a combined total tumor dose of 6,460–6,860 r at Point "A" and 3,340–3,470 r at Point "B" would be delivered in an over-all treatment

* Presented at the Fortieth Annual Meeting of the American Radium Society, Hollywood Florida, March 27–29, 1958. From the Los Angeles Tumor Institute, Los Angeles, California.

time of forty-two days. On January 1, 1956, the plan was changed to increase the daily increment of radiation from the cobalt 60 to reach a level of 3,000 r tumor dose to the midpelvis in twenty-one treatment days, while the radium applications remained the same. This, then, would deliver 7,460–7,860 r to Point "A" and 4,340–4,470 r to Point "B" in the same treatment time. Up to June 30, 1957, 14 Stage I patients were so treated.

Figure 1 is a time-dose graph showing the actual calculated doses at Points "A" and "B" for each of these 40 patients. The mean treatment time was forty-two days for the early group with mean dosage levels of 6,650 r at Point "A" and 3,400 r at Point "B." The mean treatment time was forty-one days for the later group, with 8,150 r at Point "A" and 4,350 r at Point "B" as the mean dosage levels. Although there was fairly good adherence to the proposed treatment plan, as shown by the grouping of the doses at two levels, individual variations allow for some confluence of the data.

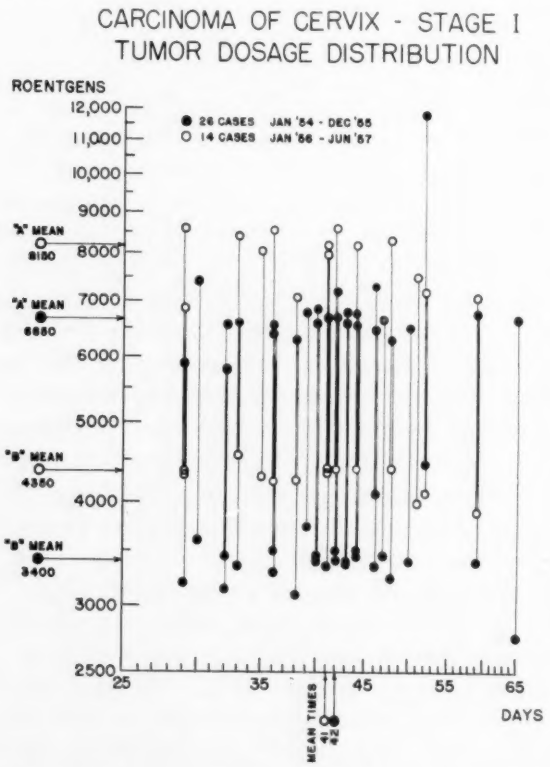

FIG. 1. Tumor doses of 40 patients, plotted on a time-dose relationship to demonstrate the range of treatment.

In Figure 2 the doses are normalized to forty-two days and arranged according to increasing dosage at Point "A." With this arrangement they show an almost continuous increase at Point "A" from 6,000 to 11,200 r; however, the Point "B" dose is discontinuous, varying from 3,000 to 4,000 r until the Point "A" dose rises above 7,000 r and then it varies between 4,000 and 5,000 r.

RESULTS

The clinical results show that in 4 patients the irradiation had failed. The dose ranges at Points "A" and "B" for each failure were: 6,150 r and 3,200 r; 6,300 r and 3,400 r; 6,850 r and 3,700 r, and 8,200 r and 4,400 r, respectively. They were distributed, then, throughout the entire curve of dosage ranges. All 4 patients were subjected to exenteration operations as a secondary treatment method. One patient in the middle of the dosage distribution did not show positive pelvic lymph nodes on histologic examination of the specimen but has subsequently expired with disease. Two of the other 3 did have demonstrable lymph node metastases but all are still alive and well.

Three patients exhibited moderate complications. One, at the lowest dose level, developed salpingitis after the first radium application and was subsequently treated by transvaginal roentgen therapy. Two others developed moderate factitial proctitis with ulceration and rectal bleeding. One of these was treated to moderate dosage and the other to 9,500 r at Point "A" and 4,800 r at Point "B"-near the extreme end of the scale.

Another method of this study involved dividing the patients into two groups, based on whether they were treated above or below 7,000 r at Point "A" in forty-two days. With such a division we found that the mean doses at Point "A" were 6,500 r and 8,050 r, and the mean doses at Point

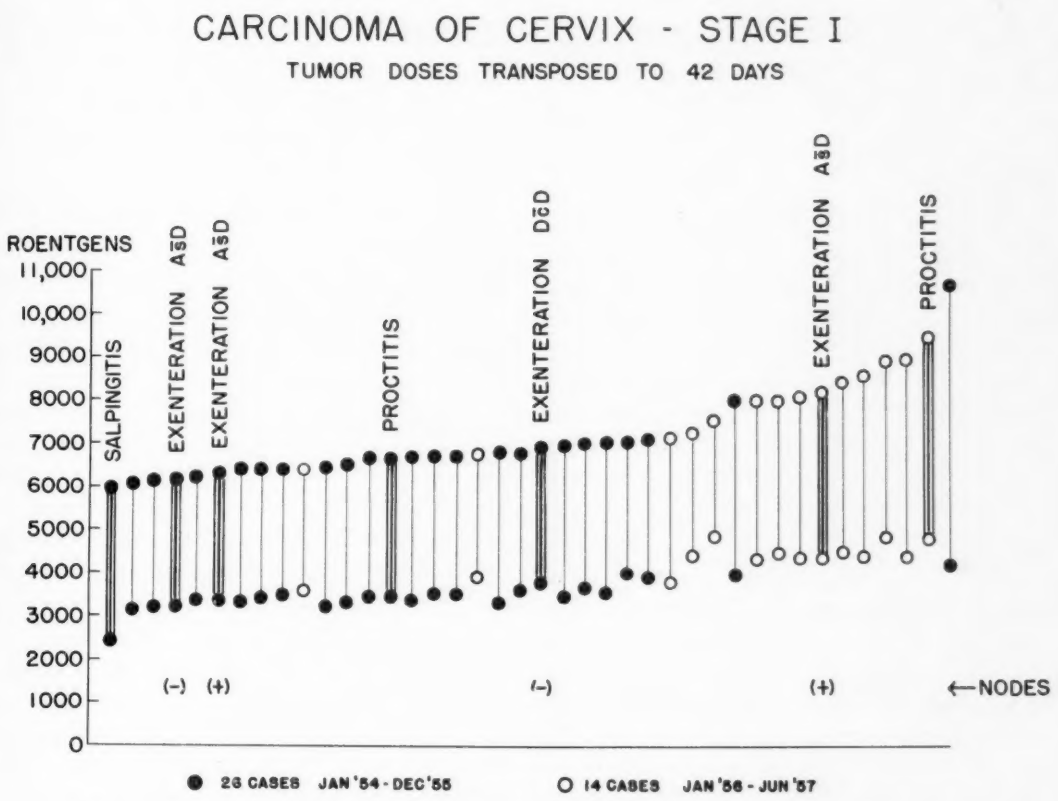

FIG. 2. Patients arranged according to normalized dose at Point "A" to demonstrate the continuity of treatment and location of complications.

"B" were 3,250 r and 4,350 r, respectively, for each group. There were 22 patients in the lower dosage group with an age range of from twenty-eight to seventy-one years, and a mean age of forty-seven years. The higher dosage group comprised 18 patients with an age range from thirty-one to seventy-seven years and a mean age of forty-five years. The histologic grade of each tumor in this group of 40 patients was not available for comparison because 11 were diagnosed only as epidermoid carcinoma, unclassified. There were two adenocarcinomas, one in each group. There were 3 carcinomas of the cervical stump in the lower dosage group and one in the group of 18 patients treated to over 7,000 r at Point "A."

In Figure 3 these groups of patients are arranged according to length of time at risk for follow-up. Those treated to lower dosage, of course, have been at risk a longer period of time. However, of the 3 treatment failures in this group, one showed clinical evidence of persistent disease and was subjected to secondary treatment by exenteration at five months. The other 2 were considered failures at eleven and thirty-one months, while the one in the higher dosage group was classed as a failure at twelve months. The patient in the low dosage group, who developed factitial proctitis, did so within the first three months after treatment, while the one patient in the higher dosage group who developed this complication did so nine months after treatment.

CONCLUSIONS

As originally stated, it would be difficult to draw any firm conclusions from these sparse data alone. It may be suggested that in this small group of Stage 1 patients, the dosage levels to which they were subjected were within a range too confined to show differences in terms of clinical results. It may be that the doses were too low to show detrimental results from high dosage at

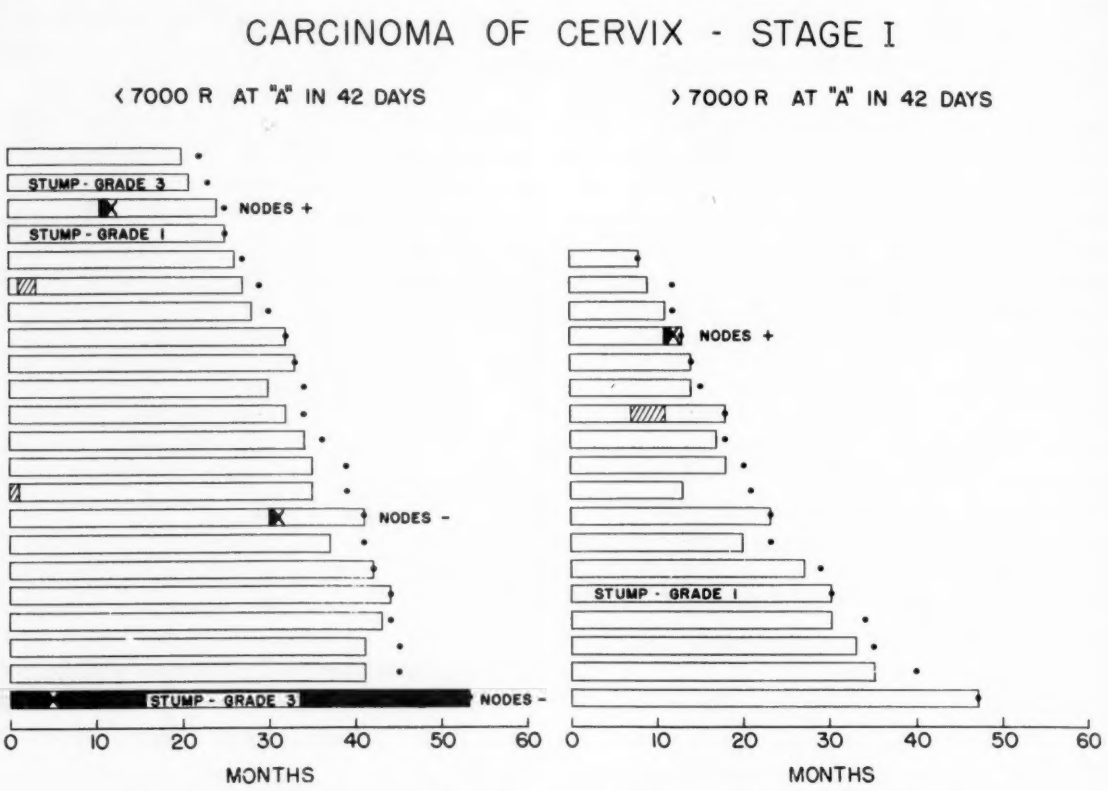

FIG. 3. Patients arranged according to time at risk for groups above and below 7,000 r at Point "A" in forty-two days, to demonstrate the results of change in treatment.

Point "A." Also, it may be said that they have not been at risk long enough to show detrimental results from low dosage at Point "B."

Certainly, there may be uncontrollable biologic factors inherent in each individual tumor or host which eventually will affect the outcome of treatment more than the treatment itself. It is conceivable that the presence of lymph node metastases, for instance, is not as much a criterion of radiation failure from a dosage standpoint as it is an indication of the biologic virulence of the individual tumor. However, since the amount and distribution of radiation therapy can be controlled, it seems wise to increase the dosage level to which a patient is subjected during primary treatment, with intent to cure, as high as is safely possible. The study of the present data has shown no increase in detrimental effects from the increase in dosage described. It seems logical to continue to treat these early lesions at least to this level. A further increase in dosage to the lateral wall of the pelvis without increasing the proximal parametrial dose, in the hope of controlling imperceptible extension of the tumor, should be considered.

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REFERENCES

1. NOLAN, J. F., VIDAL, J. A., and ANSON, J. H. Early experiences in treatment of carcinoma of uterine cervix with cobalt^{60} teletherapy and intracavitary radium. *Am. J. Obst. & Gynec.*, 1956, *72*, 789–803.
2. TOD, M. C. Optimum dosage in treatment of carcinoma of uterine cervix by radiation. *Brit. J. Radiol.*, 1941, *14*, 23–29.

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THE USE OF RADICAL SURGERY IN THE TREATMENT OF CANCER OF THE CERVIX*

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THIS paper reviews the author's own results of radical hysterectomy as a method of treating carcinoma of the cervix uteri, Stages I and II, and his rather meager explorations into the use of exenteration operations for more advanced or recurrent disease.

Before enumerating the end results obtained by radical hysterectomy, it would seem wise to caution the reader that such results are of doubtful value for comparison with those produced by radiation therapy because they are always obtained from selected series. No sensible surgeon would attempt to operate on every patient without regard to the general physical condition. Obviously, cardiovascular complications, excessive obesity or advanced age are important factors in deciding to undertake a prolonged and difficult operation. If one does not consciously select cases as being suitable or unsuitable for radical surgery, selection is still brought about by one's reputation. Referring doctors will send in only the cases they think proper subjects; patients in poor general condition will themselves refuse radical surgery.

Effect of Selection on End Results

To illustrate the effect of such selection on the results that are obtained, we would like to describe the first extensive series of radical hysterectomies in which we played an important role. In 1945 and 1946 at the Memorial Hospital, all primary untreated carcinomas of the cervix were examined, staged, and placed into two groups *by strict alternation.* At the close of this clinical experiment, 87 such patients had been seen. Of these, 43 were chosen for treatment by radical surgery and external irradiation (Table 1), while 44 were placed in a group to be treated by external irradiation and radium without surgery. Both groups had approximately equal numbers of early and moderately advanced cases: 14 Stage I and 29 Stage II cases in the first group and 13 Stage I and 31 Stage II cases in the second group. The cases for which radical surgery was planned, were selected by chance alone, their classification being determined only by the order in which they entered the hospital.

The results of this clinical study have been reported before the American Radium Society at its Thirty-fourth Annual Meeting in 1952[3] but will bear repeating as far as the "surgical series" is concerned in order to make the point clear as to what effect surgical operability may have on five year salvage statistics. Of the 44 patients treated by external irradiation and radium without surgery, 30 (68.2 per cent) were alive and apparently free of cancer at five years. Of the 43 patients designated for treatment by radical surgery and external irradiation, 24 (55.8 per cent) were alive and free of cancer at five years. These are total gross cure rates and no corrections were made for patients dying of other causes before five years.

A closer study of the "surgical group" reveals that of the 43 patients, 14 were found to be unsuitable for radical hysterectomy after they had been admitted to the hospital for preoperative work-up and surgical evaluation (Table 1). Among these, 4 were obese; 3 were hypertensive or had other medical contraindication; in 3 the disease had spread beyond the field of a radical hysterectomy as discovered by preoperative work-up; and in 3 inoperability was disclosed at the time of a surgical exploration. Unfortunately, we do not know why

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the fourteenth case was not operated upon as the record was lost or destroyed. All 14 received full external radiation therapy and radium after it was decided that they were not suitable for radical hysterectomy. Of these 14, only 2 (14 per cent) were living and apparently free of cancer at five years. Of the remaining 29 on whom radical hysterectomy was performed followed by full external radiation therapy, 22 were living and well at five years (Table I). Judging from these cases alone, surgery was eminently successful in 22 cases (76 per cent). Note that the 14 who were not considered to be suitable for radical surgery, even though their cancers were thought to be early and limited in extent, did very poorly even with full radiation treatment. Radiation therapy must accept the handicap of such cases which the surgeon can reject. For really valid evaluation of radical surgery versus radiation therapy, we believe that only strictly comparable groups of alternate cases in sufficiently large numbers treated in the same institution by the two modalities can give worthwhile statistics. So far no such studies have been done.

TABLE I

A GROUP OF 43 CASES OF CANCER OF THE CERVIX, STAGE I AND II, SELECTED FOR RADICAL SURGERY AT MEMORIAL HOSPITAL
1945–1946

Total number of cases	43
Apparently free of cancer at 5 years	24
Five year cure rate	56%
Cases actually undergoing radical surgery	29
Apparently free of cancer at 5 years	22
Five year cure rate	76%
Cases unsuitable for radical surgery	14
Excess obesity	4
Hypertension or other medical contra-indication	3
Spread of disease before operation	3
Inoperable at time of surgical exploration	3
Record missing	1
Apparently free of cancer at 5 years	2
Five year cure rate	14%

TABLE II

AUTHOR'S SERIES OF RADICAL HYSTERECTOMIES

Total number to March 1, 1958	122
Operative deaths	1
Number of hysterectomies performed before March 1, 1953	58
Apparent 5 year cures	38
Five year cure rate	65.5%
Stage I cases with hysterectomies performed 5 years ago	24
Living and well at 5 years	22
Five year cure rate	92%
Stage II cases with hysterectomies performed 5 years ago	30
Living and well at 5 years	16
Five years cure rate	53.3%

RADICAL HYSTERECTOMY IN EARLY CASES

With these reservations in mind, what personal statistics can we produce to show the results of radical hysterectomy and bilateral pelvic lymph node dissection in Stage I and II cervical cancer? From February, 1944 to March, 1958, 122 women have been subjected to radical hysterectomy (Table II). There has been in this series one operative death due to uncontrollable status asthmaticus. This was in 1947 when cortisone was not available. The patient literally died of exhaustion trying to get her breath. Two patients had developed postoperative ureterovaginal fistulas for no apparent reason. Three had fistulas as the result of wounds made in the ureter at the time of the operation. In one case this was deliberate, the ureter being cut above and below known parametrial disease and anastomosed end to end during the operation. Judging from these 3 cases, such anastomoses do not heal well nor are subsequent re-implantations in the bladder practical or successful. All 3 cases had ultimate nephrectomy. Of the spontaneous fistulas, one patient had a nephrostomy, a re-implantation of the ureter into the bladder three months later, was discharged against advice and died in the British West Indies of pyelonephritis eight months later.

The other had a nephrostomy with subsequent healing of the fistula. She now has a moderate hydronephrosis.

Fifty-eight cases were operated upon before March 1, 1953 and these are available now for five year postoperative follow-up. Of these, 38 are known to be living and well, apparently free of cancer at five years, a 65.5 per cent five year cure rate.

Of the 58, 24 were classified preoperatively as Stage I with the disease confined to the anatomic limits of the cervix. Of these, 22 (per cent) are known to be living and well at five years. One case was living and free of disease when last seen at four years. The twenty-fourth case was seen only once after her discharge from Bellevue Hospital.

There were 30 Stage II cases of which 16 (53.3 per cent) were known to be living and apparently free of cancer at five years. Ten died of cancer before five years. Three died without cancer, one postoperatively, one of pyelonephritis as already mentioned, and one at four years and ten months following an acute coronary thrombosis. One patient was lost to follow-up.

The other 4 cases were operated upon for intra-epithelial carcinoma, carcinoma of the vagina, and 2 cases for recurrent carcinoma of the cervix Stage III.

These figures are surprisingly good. To indicate that they do not represent merely one surgeon's ability to select favorable cases for radical surgery, it may be worth while to quote the simultaneous experience of the entire Gynecologic Service at Sloane Hospital as published by Frick, Corscaden, Jacox and Taylor.[2] Their figures include 21 of the 58 cases mentioned above. As indicated in Table III, 45 (86.5 per cent) of 52 Stage I cases treated by radical hysterectomy were alive at five years; 8 (42.1 per cent) of 19 Stage II cases survived five years. The comparable figures for similar cases treated by external irradiation and radium was 37 (56 per cent) of 66 for Stage I and 34 (44 per cent) of 77 for Stage II. Even making allowance for the fact that the surgical group contained more very early cases than did the radiation one, it had a better cure rate for the Stage I c cases, *i.e.*, for those with lesions of more than 1 cm. in diameter. The results were 17 out of 22 (77.3 per cent) by surgery as compared with 20 out of 40 (50 per cent) by radiation. Again we must caution against rash conclusions and point again to the Memorial Hospital series.

In the 58 cases there were 11 (19 per cent) with positive lymph nodes. Of these, 3 were apparently cured and one was lost to follow-up.

At least two conclusions can be derived from these data: First, that radical surgery is safe in properly selected patients and, secondly, that the risk of complications is small and quite acceptable in the light of

TABLE III

FIVE YEAR SURVIVAL OF CANCER OF THE CERVIX UTERI, SLOANE HOSPITAL 1944–1951 INCLUSIVE

Stage	Surgery				Radiation Therapy			
	Total	Well at 5 Years	Per Cent		Total	Well at 5 Years	Per Cent	
I a	16	14	87.5		2	1	50	
I b	14	52	14	45	100	86.5	24	66	16	37	66.6	56
I c	22		17		77.3		40		20		50	
II	19		8		42.1		77		34		44.1	
III	0		—		—		70		12		17.1	
IV	0		—		—		19		1		5.2	
Totals	71		53		74.6		232		84		36.2	
I and II	71		53		74.6		143		71		49.7	

results achieved. Certainly, there are no more disabling injuries, if as many, as would occur with adequate irradiation. Radical hysterectomy is a highly effective method of curing patients with small localized lesions when it can be carried out thoroughly and neatly. In our opinion it represents the method of choice in such cases. Cutting through gross or microscopic areas of cancer never cures and probably hastens the growth of the cancerous process. Many of the Stage II and III cases, however, are curable by radiation therapy and, therefore, this should be the preferred mode of treatment in these instances.

EXENTERATION

In 1956 Brunschwig and Daniel[1] reported a total of 441 exenterations of which 219 were complete. Although the author's personal experience with these operations is limited, perhaps conclusions which agree with larger series are worth recording.

The first total exenteration was done at the Delafield Hospital in 1951. From then until March 1, 1958, exenteration had been attempted 39 times (Table IV). In 20 of these patients, the operation was abandoned for the following reasons: in 12 there was metastatic cancer either in the para-aortic lymph nodes or elsewhere in the abdomen outside the limits of the pelvis. We do not feel that ultraradical surgery constitutes good palliation. Consequently, if metastatic disease is found above the level of the umbilicus, we make no attempt to remove it but do an exploratory laparotomy only. In 4 patients, the wall of the external iliac artery was invaded by metastatic tumor. While the external iliac vein has been removed with no serious sequelae, ligation of the artery is said to result in gangrene of the leg. In 2 patients, the tumor grew into the pelvic wall and the organs could not be freed without cutting through it and leaving some behind. In one patient, the operation was abandoned because of her narrow pelvis and excessive obesity. In one patient, an attempted two stage procedure resulted in a large abscess in the bladder and the obliteration of all cleavage planes by inflammatory reaction.

Of the 20 operations attempted and abandoned, 12 were considered radiation failures.

Nineteen patients had completed exenterations performed. Of these, 10 were total, removing the rectum, vagina, uterus, and bladder; 6 were anterior, leaving the rectum; and 3 were posterior, leaving the bladder. Thirteen of these had recurrent or persistent cancer following heavy irradiation.

As of March 1, 1958, 6 of these 19 patients were still alive. Two total exenterations have survived six years and five years after operation without recurrence. The other 4 cases are too recent for five year follow-up but 2 are thought to be cured.

We conclude from our experience that in certain cases of cancer of the cervix exenteration is a successful and worthwhile procedure. We believe it should be used only for possible cure and not for palliation. It is certainly exhausting to the patient and to the surgeon and usually financially disastrous to all concerned, hospital, doctor and patient.

Radical surgery is not the entire answer to the treatment of cervical cancer. The surgeons who have revived it, however, have made a worthwhile contribution. It probably is the method of choice in Stage I lesions in the average patient. Ultraradical surgery certainly ought to be kept in mind as a last resort in the advanced lesions.

TABLE IV

EXENTERATIONS

Total number of exenterations attempted	39
Abandoned	20
Para-aortic lymph node metastases	12
External iliac artery invasion	4
Local fixation	2
Technical difficulty	2
Operations completed	19
Anterior	6
Posterior	3
Total	10
Living (2 more than 5 years)	6

SUMMARY

1. One hundred and twenty-two radical hysterectomies have been performed from February, 1944 to March, 1958 with one death in the hospital. Five ureteral fistulas occurred, one of which was the result of the intentional resection of the ureter.

2. Fifty-eight cases have been operated upon five or more years ago. The cure rate for Stage I carcinoma of the cervix was at least 92 per cent (22 out of 24 patients), the other 2 cases being lost, one free of cancer at four years. The cure rate for Stage II was 53 per cent (16 out of 30 patients). Eleven of the 58 patients had positive metastatic lymph nodes, 19 per cent; of these 3 were cured five years or more.

3. In 39 patients with advanced pelvic carcinoma exenteration was attempted. The attempt was abandoned in 20, 12 because of metastatic disease above the level of the umbilicus and 4 because of involvement of the external iliac artery.

4. Nineteen patients have had exenterations performed, 10 being total, 6 anterior, and 3 posterior. Of these, 6 are still alive, 2 for more than five years.

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REFERENCES

1. BRUNSCHWIG, A., and DANIEL, W. Evaluation of pelvic exenteration for advanced cancer of cervix. *Surg. Gynec. & Obst.*, 1956, *103*, 337–341.
2. FRICK, H. C., II, CORSCADEN, J. A., JACOX, H. W., and TAYLOR, H. C., JR. Surgical and radiological treatment of cancer of cervix; review of 397 cases treated from 1944 to 1951 at Sloane Hospital and Francis Delafield Hospital. *Surg., Gynec. & Obst.*, 1958, *107*, 457–468.
3. TWOMBLY, G. H., and TAYLOR, H. C., JR. Treatment of cancer of cervix uteri; comparison of radiation therapy and radical surgery. AM. J. ROENTGENOL., RAD. THERAPY & NUCLEAR MED., 1954, *71*, 501–508.

RESULTS OF RADIATION TREATMENT OF CARCINOMA OF THE CERVIX IN A SMALL HOSPITAL

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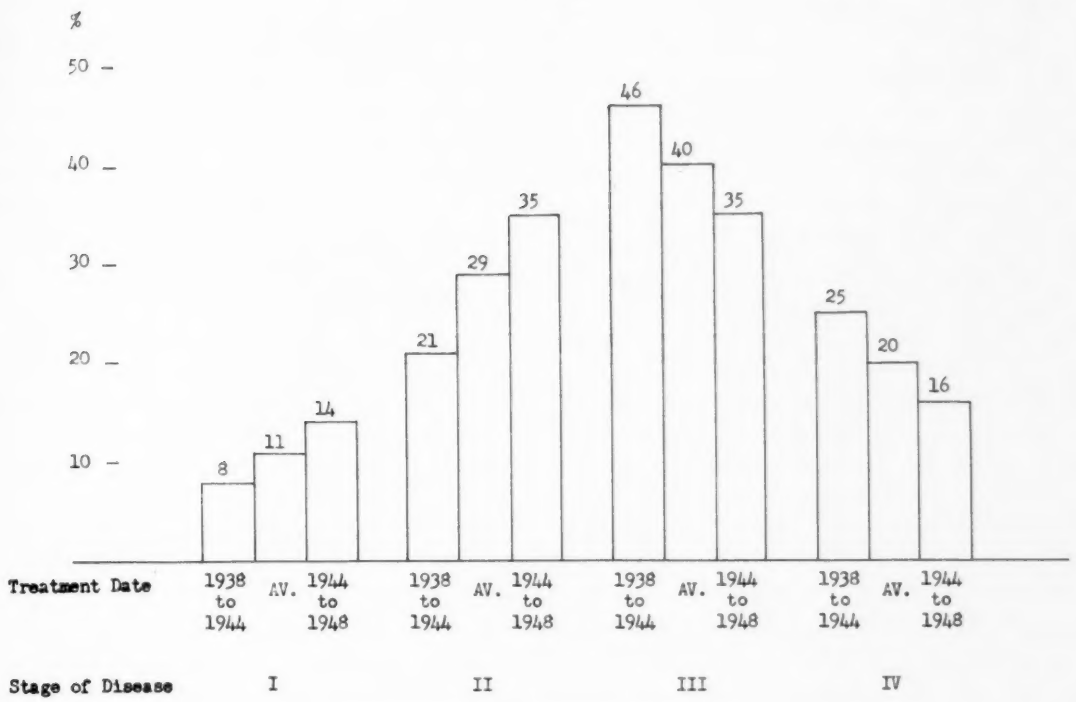
THIS statistical review of irradiated cervical carcinoma was undertaken in order to provide a control series against which we may compare eventual results of a series of similar unselected cases to be treated by a different method of irradiation technique than heretofore used. In the period from January, 1938 to July 1, 1948, 162 cases of cervical carcinoma were seen and treated in our department. Of these 2 were not included in this series. Both of these excluded cases lived five or more years. One was a true carcinoma *in situ* and the other was excluded because of insufficient records for staging. Of the 160 cases comprising this series, 7 either died of intercurrent disease or were lost to follow-up before five years had elapsed, and will be discussed at the appropriate point in this paper. Between May 15, 1944 and July 1, 1948 the records in this department include the calculated tumor dose at the midpelvis. Prior to 1944 this information could not be accurately obtained from the records available, and most patients received a standard dose of 11,200 r as measured in air through four pelvic portals, decreasing in area as the treatment proceeded. Transvaginal roentgen therapy was not employed prior to 1944 and roentgen dosage was not recorded in terms of tumor dose. Therefore, we have arbitrarily divided this series of cases into two groups,—those treated between January, 1938 and May 15, 1944, and those treated between May, 1944 and July 1, 1948.

Not all of the patients could by any stretch of the imagination be considered to have received optimum treatment. As an example, in the 1944–1948 group 1 patient failed to continue her treatment, receiving a total of only 475 r calculated tumor dose. This patient died within a few months, but is included for statistical purposes as a treatment failure. A number of other cases likewise failed for one reason or another to complete what we considered to be an optimum course of treatment.

During this ten year period no detailed or complicated dosage measurements were taken. However, after May, 1944 anteroposterior measurements of the pelvis were obtained and minimum tumor dose at the mid-pelvis was calculated by summation of the percentage depth doses as determined from Quimby's depth dose tables. In the 1944–1948 period an attempt was made to deliver through external portals a minimum of 4,000 r, and preferably 4,400 r, at the mid-pelvis. Portal size ranged from 8 by 10 cm. up through an occasional case treated with 15 by 15 cm. portals. The great majority of patients were treated with four 10 by 10 cm. pelvic portals, all being directed through the mid-pelvis. Roentgen radiation was generated at 200 kv. peak with a half-value layer of 1.2 mm. Cu and a target skin distance of 50 cm. Occasionally additional roentgen radiation was administered through perineal portals in order to reach the goal of 4,000 r minimum. During this period great insistence was always placed on careful and meticulous positioning of treatment portals. Portal position was checked at intervals by means of roentgenograms taken with the therapy tube.

Table 1 is a bargraph indicating the distribution by stage of disease. The League of Nations classification was employed. From a study of this graph it will be noted that during the 1944–1948 period there was a tendency to stage the disease earlier. This, all other factors being equal, would, of course, tend toward somewhat poor percentage results in all stages. However, as can be seen by a study of Table II, such did not prove to be the case, but there was an

TABLE I



PERCENTAGE DISTRIBUTION BY STAGES

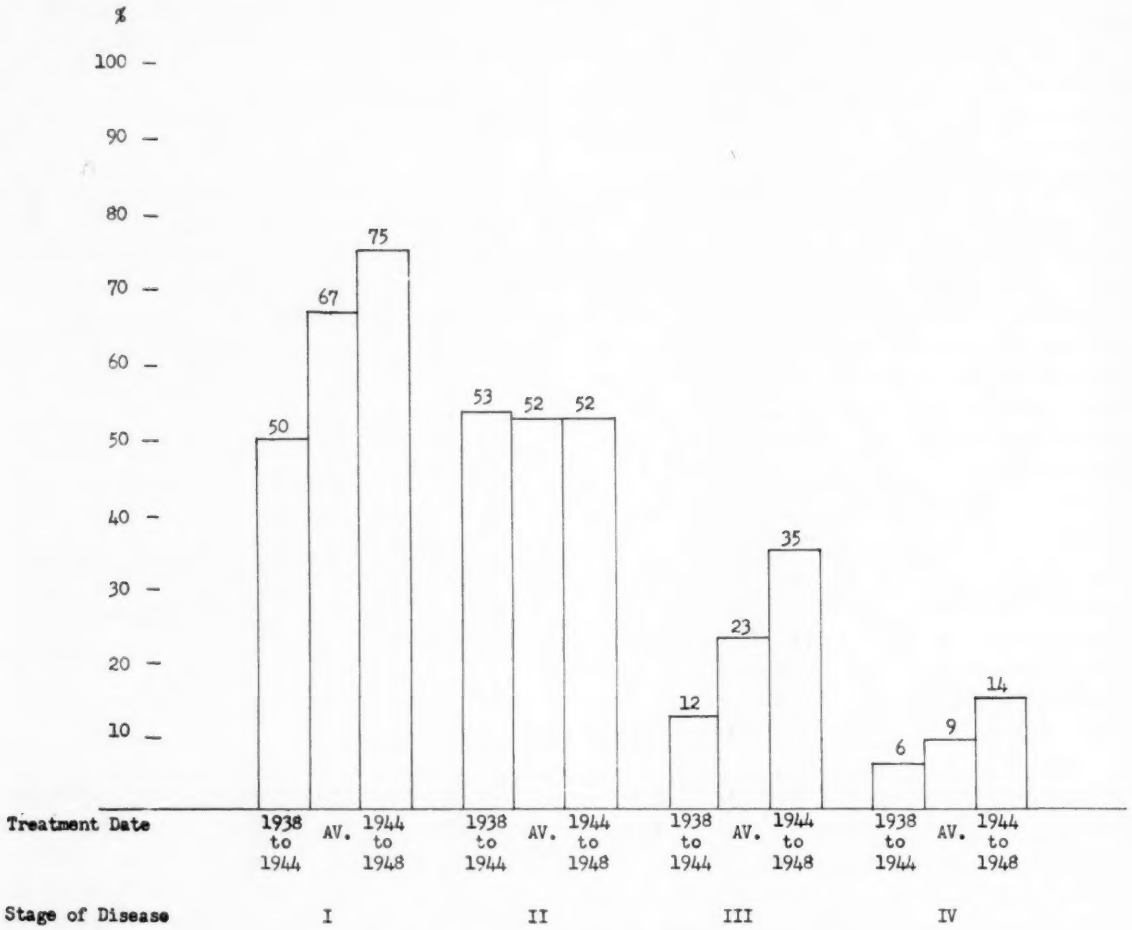
absolute increase in the five year survival rate.

Of the 7 cases lost to follow-up (but counted as failures), 3 were treated in the 1938–1944 period. Of these 2 were in Stage I. One was lost to follow-up after three months, the other died of intercurrent disease (cerebral hemorrhage at the age of sixty-seven) without evidence of malignancy during the third year after treatment. A third patient lost to follow-up in this group was classified as Stage III and was lost to follow-up within six months after treatment.

Of the 4 cases lost to follow-up treated in the 1944–1948 period, 2 were classified as being in Stage I. The first died of intercurrent disease at the age of sixty-nine without evidence of malignancy two years and five months after treatment. The second died of intercurrent disease (heart attack) at the age of fifty-seven without evidence of malignancy after three years. The remaining 2 cases were classified as Stage III when treated. One of these was known to have been living two years following treatment, but we have been unable to obtain any information as to her condition. She was subsequently lost to follow-up. The other was completely lost to follow-up immediately following treatment and all efforts to trace her have been to no avail.

If we assume that all 7 of these were failures, then the absolute five year survival rate for the entire ten year period is 34 per cent. If we exclude these in the series, the absolute five year survival rate becomes 36 per cent. In comparing the earlier with the later series, we obtain a five year survival rate of 22 per cent for the 1938–1944 period if the cases lost to follow-up are included as failures. This becomes a 23 per cent five year survival rate if they are excluded. In a later series between 1944–1948 the five year survival rate is 43 per cent if we include the cases lost to follow-up as failures. If they are excluded it becomes 45 per cent. Obviously, the true percentage result lies between these two figures. The above information in the form of a bargraph is

TABLE II



PERCENTAGE FIVE YEAR SURVIVAL BY STAGE OF DISEASE
(INCLUDING AS DEAD 7 PATIENTS LOST TO FOLLOW-UP—SEE TEXT)

presented in Table II.

As was stated earlier in this paper our goal in each of the cases in the 1944–1948 group was administration of a minimum of 4,000 r mid-pelvic dose through external portals, supplemented by transvaginal roentgen therapy to the cervix and adjacent parametria to an average tissue dose in mid-cervix of approximately 3,000 r, or an equivalent dose by the use of radium. It is of interest to note that in the 1944–1948 series there was no survival when this minimum for external roentgen therapy was not obtained, even though in many cases additional irradiation by means of radium and transvaginal roentgen therapy was employed. There was an insufficient number of patients in the various groups, as well as insufficient data to warrant any general assumption as to the efficacy of radium versus transvaginal roentgen therapy as a supplement to the external irradiation. Some of these cases had both transvaginal roentgen therapy and radium therapy. Furthermore, the radium dosage was applied in a variety of distributions and recorded only as milligram hours.

In the Stage II cases the employment of radium as supplement to the roentgen therapy did not appear to influence the results in any appreciable degree as compared with the use of transvaginal roentgen irradiation.

Dosage data on the cases treated prior to

1944 are inadequate to allow for any evaluation or assumption.

In Stage I during the entire ten year period there was 1 patient who received only external radiation which was not supplemented by either transvaginal roentgen irradiation or radium therapy. This patient, it is interesting to note, is now dead but she lived for five and one-half years and then died with disease.

In Stage II there were 8 patients who received no transvaginal roentgen irradiation or radium therapy. Of these, 1 female, aged sixty-three, is still living six years after treatment, but with evidence of some residual disease. Another patient, aged fifty-six, who received a calculated minimum tumor dose of 4,000 r, but no transvaginal roentgen irradiation nor radium therapy lived for five years but died with evidence of disease immediately after her fifth year. Another patient, aged seventy-three, was treated early in 1944 with a calculated minimum tumor dose of 3,540 r; no additional radiation through a transvaginal portal nor radium was administered. She was followed for five years, but has since been lost to follow-up. We do not know her present condition. A fourth patient in the Stage II group was sixty-nine years of age at the time of treatment, receiving a calculated tumor dose of slightly more than 4,000 r. This patient survived for five years and then died from intercurrent disease without evidence of malignancy. A fifth patient in the Stage II group without radium or transvaginal roentgen treatment was thirty-eight years of age at the time of treatment in 1945. She survived seven years but died after that time with evidence of recurrent disease. Three cases, aged thirty-seven, fifty-three and seventy-seven, respectively, receiving external irradiation only, died within a year following treatment, with the disease uncontrolled.

Thirteen patients in Stage III received only external irradiation. Two of these lived for five or more years without evidence of disease following treatment. One has now lived eleven years without evidence of disease. This patient had a squamous carcinoma of the cervix, Stage III, arising in a cervical stump. She had had a subtotal hysterectomy at the age of twenty-four years. She was fifty-one years of age at the time of treatment in 1941. The other one surviving was forty-nine years of age at the time of treatment. Her treatment with a minimum mid-pelvic dose of 4,200 r was followed after thirty days by a panhysterectomy. She went five years without evidence of residual or recurrent disease but has since been lost to follow-up. Of the remaining 11, 5 received less than 4,000 r at the mid-pelvis and all of these died before one year had elapsed following therapy. One of these received less than 850 r, another received only 1,675 r. The other 6 received 4,000 r or better, but without transvaginal roentgen therapy or radium therapy. All of these died within an eighteen month period following treatment.

Of the 20 Stage IV patients who received only external irradiation, 1 lived for five years and five months but with evidence of disease. Another patient found in this category of external irradiation with a minimum tumor dose somewhat above 4,000 r to the mid-pelvis, no radium or transvaginal roentgen therapy, is still alive and well seven years after treatment. This patient also had a carcinoma in the cervical stump. A supracervical hysterectomy was done approximately nine months prior to radiation treatment for carcinoma of the cervical stump and pelvis. A third patient falling in this group received a calculated mid-pelvic dose of 3,138 r in 1944. This was in the cervical stump, the patient having had a hysterectomy in 1919. She is still alive, well, and working more than eight years after treatment. Perhaps one should question the accuracy of the original staging in view of such results. However, it should be noted that the majority of this entire series were staged by at least two consultants and the recorded staging agreed upon by such consultants. In any event, in

such a statistical review we must report recorded findings. In this Stage IV group the other 17 died within less than one year and eight months following treatment, most of them within the first nine months.

CONCLUSION

This study points up the value of individual consideration, measurement, and careful calculation of radiation dosage for each patient. There was no change in equipment available during the entire ten year period.

Although the series is small, it suggests that results are less dependent upon the source or nature of irradiation employed than on a thorough knowledge of the disease and an acquaintance with the fundamental principles of radiation therapy in its broadest aspects. For example, it was apparent that transvaginal roentgen irradiation, properly employed in properly selected patients was neither inferior nor superior to radium therapy.

The five year survival rate must not be confused with cure rate as witness those patients in this series surviving five years but with demonstrable evidence of disease. There exists the question of how many more of these five year survival patients have disease which is not at present demonstrable.

By indicating distribution of material according to stages, varying series of cases may be more accurately compared, yet the variation in estimates of stage by different individuals will still tend to raise a question as to the accuracy of comparing results not only in individual stages but even in entire unselected series.

The crude five year survival rate seems to us a most important index of success in treatment, but this also may be affected in various series by reason of age distribution, social economic status, and other factors.

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BILATERAL URETERAL OBSTRUCTION COMPLICATING THE TREATMENT OF CARCINOMA OF THE CERVIX*

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THE frequent involvement of the urinary collecting system in cases of carcinoma of the cervix is a well documented observation.[2,3,5,6,7,9] Both bladder and ureters are subject to invasion by direct extension of the neoplasm. The effect upon the ureters is invariably one of partial or total occlusion to the degree of producing hydronephrosis, a nonfunctioning kidney, or in the event of infection, pyelonephritis or pyonephrosis. It becomes apparent that this involvement is of significance when one realizes that among two-thirds to three-fourths of those who die with carcinoma of the cervix the cause of death is more related to urinary tract complications in the form of pyelonephritis or renal failure than to the far reaching effects of the neoplasm *per se*.[1–4,9]

This information should not suggest that if the urinary tract involvement were eliminated, the cure rate would improve. When renal failure develops following radiation therapy, the cause is almost always due to recurrent tumor in the pelvis and is not commonly due to inflammatory or radiation strictures of the ureters[2,4,5,6,8,9] so if the urinary tract complications were removed from the scene, the neoplasm would still eventually determine the fate of the individual.

Furthermore, urinary tract involvement prior to treatment appears to be an ominous prognostic finding. Todd[10] reported 21 cases out of 32, or 66 per cent, of carcinoma of the cervix with ureteral involvement prior to treatment dying within one year of treatment. Among 102 cases of carcinoma of the cervix at this institution exhibiting abnormal intravenous pyelograms before treatment, 54 (54 per cent) were dead one year following completion of therapy. Table I gives the treatment results of two series of cases of comparable clinical staging according to the presence or absence of ureteral involvement before treatment. In the series without involvement, 45 of 196 cases (23 per cent) of Stage III and IV carcinoma of the cervix survived five years. Of 94 cases of Stage III and IV carcinoma of the cervix with ureteral involvement prior to treatment, only 6 cases (6.4 per cent) survived five years.

This observation is further confirmed by Spence and Hare,[9] in whose series of 100 consecutive cases of carcinoma of the cervix 11 showed ureteral obstruction prior to treatment and 16 developed obstruction during treatment. None of these cases survived five years.

Urinary tract involvement prior to treatment will occasionally determine whether radiation therapy can be administered at all. Individuals with anemia, uremia and pyelonephritis tolerate radiation therapy

TABLE I

EFFECT OF URETERAL INVOLVEMENT BY CARCINOMA OF THE CERVIX UPON PROGNOSIS

	Without Involvement			With Involvement		
Stage	No. Cases	5 Year Survival	Per Cent	No. Cases	5 Year Survival	Per Cent
III	88	30	34	38	3	8
IV	108	15	14	56	3	5.4
Total	196	45	23	94	6	6.4

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† Chief Surgeon.
‡ Radiotherapist.

poorly and it is in these particular cases that the opportunity to render treatment is often dictated by the status of the urinary tract rather than by the status of the neoplasm.

Recently, 2 cases of carcinoma of the cervix were treated at this institution in which ureteral involvement by the neoplasm produced obstructive renal failure to the extent that radiation therapy could not be continued. Summaries of the hospital course and management of these two cases follow:

REPORT OF CASES

CASE 1. L.M., a forty-nine year old white female housewife, was admitted to the Ellis Fischel State Cancer Hospital for the first time on March 11, 1955 with vaginal bleeding of four months' duration. Her temperature was 98°F., pulse rate 80, and respiration rate 22. The blood pressure was 110/70. She appeared chronically ill and slightly anemic. An exophytic tumor occupied the cervix and obliterated the anterior and both lateral fornices. Both parametria were infiltrated to the pelvic wall. Cystoscopy was negative for bladder invasion. The lesion was classed as a clinical Stage III epidermoid carcinoma of the cervix. Intravenous pyelography on admission revealed nonfunction of the left kidney and decreased function of the right kidney with marked hydronephrosis and hydroureter.

External roentgen therapy was begun on April 13, 1955 through six pelvic ports. Three weeks after initiation of therapy the patient developed anuria. The blood urea nitrogen at that time was 42 mg. per cent. Radiation therapy was discontinued and a ureteral catheter was passed into the right renal pelvis, past a strictured area near the ureterovesicular junction and 4,400 cc. of clear pale urine was obtained in the first twenty-four hours. The left ureter could not be located at cystoscopy. Four days later the catheter was spontaneously extruded and was reintroduced into the right renal pelvis. However, it functioned poorly for the next twenty-four hours and during this time the patient was quite ill with nausea, vomiting, fever, tachycardia and pelvic pain. Laboratory studies at the time revealed a hemoglobin of 9.3 gm., blood urea nitrogen 32 mg. per cent and normal serum electrolytes. Within twenty-four hours the catheter again was extruded and additional attempts to pass it were unsuccessful.

The patient had remained anuric during the periods when the catheter was not functioning. Accordingly, an emergency nephrostomy was carried out after blood and fluid replacement. The right kidney was hydronephrotic and good drainage through a flank wound was established. Exploration of the left flank revealed an apparent absence of the left kidney. Following nephrostomy a rapid and progressive improvement ensued with copious diuresis for a forty-eight hour period. The blood urea nitrogen quickly returned to normal and the patient resumed normal alimentation with considerable subjective improvement. Radiation therapy was resumed two weeks following the nephrostomy and carried to completion. This included radium application in the form of an intrauterine tandem and later in the form of a colpostat. Ten days following nephrostomy the patient began voiding small amounts of urine via the bladder. As radiation therapy progressed, the amount steadily increased with a concomitant decrease in the volume collected from the nephrostomy tube. Six weeks following nephrostomy the nephrostomy tube was clamped and the occlusion was tolerated well. Repeat intravenous pyelography two months following nephrostomy showed good function with marked diminution in the hydronephrosis of the right kidney. The nephrostomy tube was removed with spontaneous closure of the urinary fistula and complete resumption of normal urination. The patient was discharged four months following admission with considerable clinical regression of the neoplasm.

Her progress was observed at frequent intervals in the outpatient department for eighteen months and she did well in all respects with no subjective complaints and no clinical evidence of recurrent neoplasm until May, 1957, at which time she was re-admitted to the hospital with marked anemia, urinary frequency, urgency and nocturia, and clinical evidence of pelvic recurrence of the neoplasm producing a "frozen pelvis."

On admission her hemoglobin was 6 gm. and the blood urea nitrogen was 140 mg. per cent. Serum electrolyte studies revealed a marked metabolic acidosis with a slight elevation of serum potassium. Biopsy of the cervix confirmed the impression of recurrent carcinoma.

Since the patient's only subjective complaints were related to her obstructive uropathy and not to the neoplasm *per se*, it was elected to perform a urinary diversion procedure in the form of a cutaneous ureterostomy. This was carried out on June 12, 1957 after correction of her anemia and acidosis. At laparotomy the congenital absence of the left kidney was confirmed. The pelvis was totally occupied by a fixed neoplasm and no distant metastases were noted. The right ureter was 4 cm. in diameter. It was divided and delivered through a right flank incision. During the first twenty-four hours 5,000 cc. of urine was obtained. The patient showed marked clinical improvement with return of the blood urea nitrogen to normal. She did well until the fifth postoperative day, at which time she expired suddenly in bed. No autopsy was obtained and the cause of death was presumed to be pulmonary embolus.

Case II. P.McC., a fifty-six year old white female housewife, was admitted to the Ellis Fischel State Cancer Hospital on September 11, 1957 with pain in the back radiating to the left groin of three weeks' duration and a profuse vaginal hemorrhage of five days' duration. Associated complaints were anorexia and a weight loss of 25 pounds over the past six weeks. Her temperature was 98.6°F., pulse rate 80, respiration rate 20, and blood pressure 210/110. The patient appeared chronically ill and anemic. The cervix was replaced by a friable, ulcerovegetant tumor which involved all the fornices of the vagina and extended into the parametria to the pelvic walls bilaterally. The uterus was twice the normal size. Cystoscopy revealed the bladder to be uninvolved and the lesion was classed as a Stage III epidermoid carcinoma of the cervix. Laboratory data on admission revealed a hemoglobin of 9.5 gm. and a blood urea nitrogen of 61 mg. per cent. Intravenous pyelography demonstrated nonfunctioning kidneys.

External roentgen therapy was begun and four days later the patient became oliguric. The blood urea nitrogen at this time was 100 mg. per cent with a marked metabolic acidosis. Roentgen therapy was discontinued and the anemia and acidosis corrected by parenteral therapy.

Based on the experience of Case I, it was felt that temporizing measures with retrograde catheterization would be of only transient benefit and bilateral nephrostomies were therefore carried out on September 23, 1957. Both kidneys were hydronephrotic and good drainage was established bilaterally with diuresis of 5 to 6 liters of urine per day for the first four days postoperatively. The patient exhibited marked subjective improvement with serum chemistries and the blood urea nitrogen reverting to normal within one week. Two weeks later radiation therapy was resumed and was continued to completion with the inclusion of radium applications in the form of an intracavitary tandem and a colpostat. The patient's hospital course was further complicated by the development of severe generalized exfoliative dermatitis occurring six weeks following admission, presumed to be secondary to allergy to penicillin. Management and eventual resolution were achieved primarily by the use of ACTH gel. During the episode of dermatitis an additional complication of spontaneous thrombosis of the right ulnar artery occurred and produced a cold, mottled and painful hand for a period of three days. This eventually limited itself to dry gangrene of the tips of the index, middle and ring fingers and this finally sloughed spontaneously to produce a minimal loss of soft tissue. No specific therapy other than stellate ganglion block was carried out for this complication.

Again, as radiation therapy progressed, the volume of bladder urine gradually increased to the point where the majority of urinary drainage was by the normal route. Six weeks following nephrostomy the nephrostomy tubes were clamped and the patient tolerated this procedure satisfactorily. Ten days following clamping they were removed with spontaneous closure of the urinary fistulae. At the time of discharge, three months following admission, the patient was experiencing normal urinary function and her serum electrolytes and blood urea nitrogen were normal. Serum chemistries studied six weeks following discharge were normal.

DISCUSSION

Though Case I succumbed to a recurrence of her neoplasm, as might have been predicted from the extent of original involvement, she was afforded an eighteen month period of relatively comfortable existence by the management just presented. It is not our policy to routinely divert the urinary stream in post therapy recurrent cases unless a pelvic exenteration

is carried out. In this case it seemed to be indicated in that the only symptom originated from the urinary tract involvement. It appears certain that a much earlier demise would have taken place had not the complication of renal failure been forestalled at the time of original treatment.

Case II is, of course, too recent for evaluation of results. Here again, the nature and original extent of the tumor implies an unlikely chance of permanent control. However, the application of the benefits of radiation therapy was made possible only after the adjuvant of urinary diversion, whereas this individual was doomed by renal failure had not temporary nephrostomies been performed.

Renal failure due to ureteral obstruction prior to treatment of carcinoma of the cervix appears to be uncommmon. Of 767 cases treated at the Ellis Fischel State Cancer Hospital over a thirteen year period, 102 or 13 per cent of the cases had evidence of urinary tract involvement demonstrated by intravenous pyelography before treatment by radiation therapy. Among these only the 2 cases presented above developed renal failure to the degree that interruption of radiation therapy was necessary.

No detailed account of this problem has been found in the literature. It is hoped that the management described above may be considered in the future treatment of these infrequent but complex clinical problems. It is not anticipated that any appreciable improvement in the survival figures will result. The number of appropriate cases are too few and the particular benefits obtained will probably be temporary at best due to the nature of the underlying disease. But at least the most common mode of exitus in patients with advanced carcinoma of the cervix shall have been forestalled until the optimum benefits of radiation therapy can be applied.

The startling and grim relationship of pretherapy ureteral involvement and a 54 per cent mortality within one year of treatment, re-emphasized when our case material was studied in preparation of this publication, suggest that a more aggressive method of primary treatment may be indicated in certain cases of advanced carcinoma of the cervix. The management of those cases with hydronephrosis or a nonfunctioning kidney on admission is currently under re-evaluation at this institution.

SUMMARY

1. Urinary tract involvement by carcinoma of the cervix accounts for two-thirds to three-fourths of the deaths in this disease.

2. The mechanism of ureteral involvement following radiation therapy is due almost always to recurrent neoplasm in the pelvis rather than to inflammatory or radiation strictures of the ureters.

3. Urinary tract involvement before treatment materially affects the prognosis.

4. Two case histories are presented in which the extent of ureteral involvement and renal failure prior to treatment required urinary diversion before radiation therapy could be administered. The clinial course and management of these cases are given in detail.

5. The successful management of such cases requires the close cooperation and mutual efforts of both the radiotherapist and the surgeon.

6. The poor outlook for individuals with pretherapy urinary tract involvement suggests that a more aggressive primary treatment for these cases may be in order.

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REFERENCES

1. AUSTER, L. S., and SALA, A. M. Causes of death in cancer of cervix uteri. *Surg., Gynec. & Obst.*, 1940, *71*, 231–239.
2. BEACH, E. W. Urologic complications of cancer of uterine cervix. *J. Urol.*, 1952, *68*, 178–189.
3. COLBY, F. H. Urinary tract complications from uterine cancer. *New England J. Med.*, 1933, *209*, 231–232.
4. DREXLER, L. S. Ureteral obstruction in carcinomatous cervix. *Radiology*, 1935, *25*, 315–318.

5. Graves, R. C., Kickham, C. J. E., and Nathanson, I. T. Ureteral and renal complications of carcinoma of cervix. *J. Urol.*, 1936, *36*, 618–642.
6. Howes, W. E., and Strauss, H. Significance of urological surveys in cervical carcinoma. Am. J. Roentgenol. & Rad. Therapy, 1939, *41*, 63–68.
7. Pomeroy, L. A. Examination of urinary and lower intestinal tracts before treatment of carcinoma of cervix uteri. Am. J. Roentgenol. & Rad. Therapy, 1947, *57*, 453–454.
8. Seaman, J. A. Urological complications of carcinoma of cervix—appraisal of 149 cases. *Urol. & Cutan. Rev.*, 1940, *44*, 740–744.
9. Spence, H. M., and Hare, D. M. Ureteral obstruction associated with carcinoma of cervix. *J. Urol.*, 1949, *62*, 219–224.
10. Todd, T. F. Urological complications of carcinoma of cervix. *J. Obst. & Gynec. Brit. Emp.* 1941, *48*, 334–353.

TRANSVERSE LAMINAGRAPHY: THE THIRD DIMENSION IN BODY SECTION ROENTGENOGRAPHY: APPLICATIONS IN RADIATION THERAPY*

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IN THE planning of roentgen therapy for patients with deep seated cancer, it becomes necessary to construct an accurate graphic cross-section of the patient's body at the treatment level for localization of the tumor, selection of portals, orientation of beams and calculation of dosage. On this effort may depend, in large measure, the probability for cure of a radiocurable cancer as well as the fate of normal structures in the path of the beam. The completed treatment plan then becomes a permanent and valuable graphic record for teaching, clinical investigation and further improvement of the level of technique for similar lesions. In our opinion, transverse laminagraphy can make a major contribution toward the accomplishment of these several objectives in radiation therapy.

In conventional practice, the radiologist begins the preparation of the body cross-section with a tracing of the patient's contour at the selected level. We use a strip of plaster bandage for this purpose (Fig. 1, *A* and *B*). The tumor and normal structures are then usually introduced by free-hand drawing with the aid of a standard anatomic cross-section atlas as well as the patient's roentgenograms. The conventional roentgenographic studies may fail to delineate the volumetric limits of the tumor, even when vertical laminagraphy in the coronal and sagittal planes can be utilized. Furthermore, the morbid anatomy of the sectioned cadaver (from which the atlas is drawn) rarely matches the living anatomy of the cancer patient under consideration. The normal relationships of organs may be grossly distorted in the cadaver as a result of collapse, especially in the thorax and abdomen. In the living patient, organ displacement produced by the tumor further complicates the problem of accurate graphic reconstruction from the atlas. In spite of laborious and time-consuming effort, the final product may be crude and misleading

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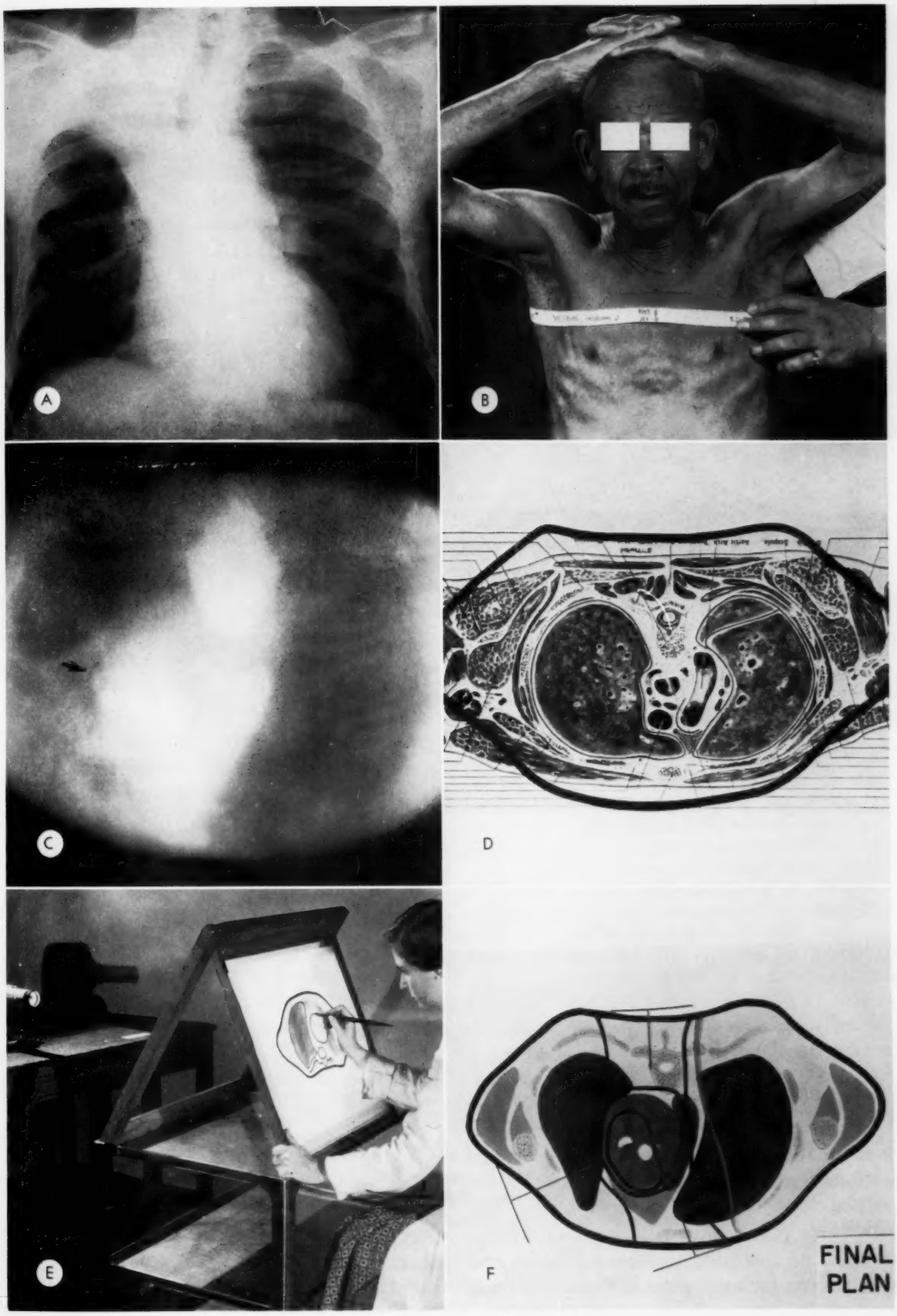
FIG. 1. (*A*) W.W., a sixty-seven year old carpenter with epidermoid carcinoma of the right upper lobe bronchus. The tumor is obscured by the atelectatic lobe. No distant metastases were present and his general condition was good. He was to receive 5,000 r in five weeks, using supervoltage roentgen therapy (1 mev.). (*B*) The body contour is molded through the principal horizontal treatment plane, using a strip of plaster bandage (resin-impregnated and fast-setting). (*C*) Transverse laminagram at treatment level, T5–6. Note demonstration of atelectatic right upper lobe distinct from dense core of tumor. The arch of the aorta is clearly delineated. Note also the shift of the left lung across the midline. Now a dependable basis is provided for an ideal treatment plan. (*D*) Tracing of the patient's contour overlaid on an atlas drawing at the same anatomic level (T5–6). Note the discrepancy in contours. Compare with laminagram of living patient in Figure 1*C* (adjoining) and note the gross disparities in spatial relationships. (*E*) The image of the transverse laminagram (in lantern slide form) is now projected upon the traced contour of the patient. The tumor and important normal structures are being traced in on a translucent planning sheet. (*F*) Final treatment plan evolved from graphic cross-section, indicating portal selection, beam orientation, and isodose distribution. A central zone around the tumor receives 5,000 r, while an outer zone (involving normal lung) receives only 1,000 r. The technique includes 1 mev. radiation, half-value layer of 3.9 mm. lead, 70 cm. target-skin distance and a dose-time formula of 5,000 r in five weeks.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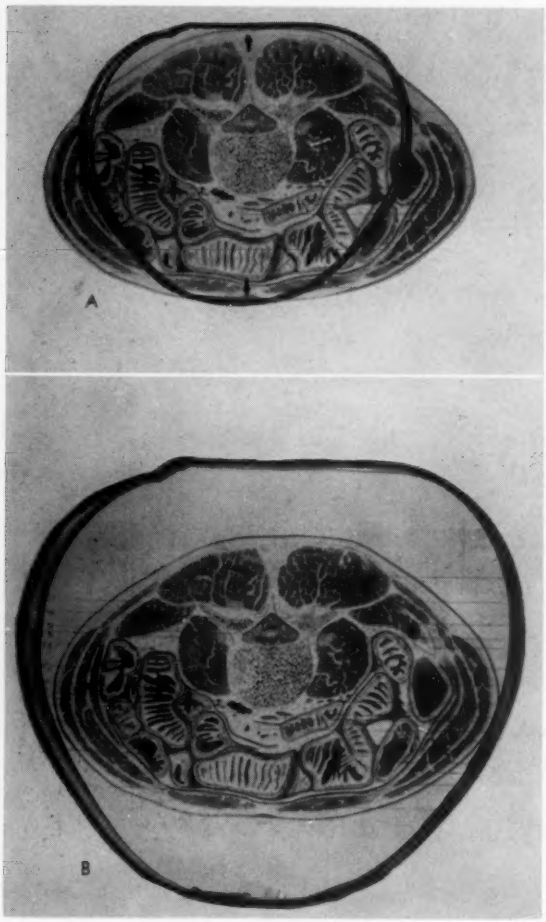

FIG. 2. (*A*) Illustration of discrepancy between morbid and living anatomy. Overlay of actual plaster contour of a patient at the level of L-4 upon an anatomic atlas cross-section at the same level. In this illustration an attempt was made to fit these two elements in the anteroposterior dimension, but the lateral margins simply do not fit. (*B*) Illustration of striking disparity between the same contour of the living patient and the same atlas cross-section, when an attempt is made to match the two units in the lateral dimension.

—hardly a sound basis for an effective treatment plan (Fig. 2).

SOLUTION OF THE PROBLEM

To overcome these objections, one should provide the patient's own anatomic cross-section. This can be accomplished by means of body-section roentgenography in the transverse plane (Fig. 1*C*). In 1954, an apparatus for this function was designed and constructed for use in our Radiation Clinic, based upon data published by Watson, Vallebona, Amisano, Gebauer and many others in the European medical literature (Fig. 3*A*).[1–9,12–18]

It soon became apparent that this technique could prove valuable not only in treatment planning, but also in localization of both benign and malignant lesions in the so-called "dark" areas of the body. Furthermore, it opened for us an exciting new frontier for exploration of normal roentgen anatomy in the living individual in the transverse or third dimension, a view hitherto accessible only to the anatomist in postmortem material.

Preliminary studies with our own equipment in phantoms and in patients proved so fruitful that an improved commercial apparatus was acquired as soon as it became available (Fig. 3*B*). It is a curious fact that this roentgenographic modality has thus far gained little interest in this country, although it has been described for more than twenty years by British, Italian, German, French and Scandinavian authors.[1–9,12–18]

PRINCIPLE

The roentgen tube remains stationary, angled downward 25° toward the film (Fig. 3, *C* and *D*). The patient and the film, on two separate stands, rotate simultaneously through 360° in the same direction and at the same rate of speed during exposure. The points of all structures in the selected plane (a–b) remain centered on identical points on the film (a′–b′) giving sharply defined stationary images. The points of all structures (X) situated outside the selected plane cast only moving shadows on or off the film and are therefore blurred or not reproduced.

TECHNIQUE

Laminagraphy in the transverse plane demands painstaking care in every technical detail. The most critical factor is the precise alignment of the tube focus with the axis of rotation of the patient and the film cassette stand. If the tube stand is also

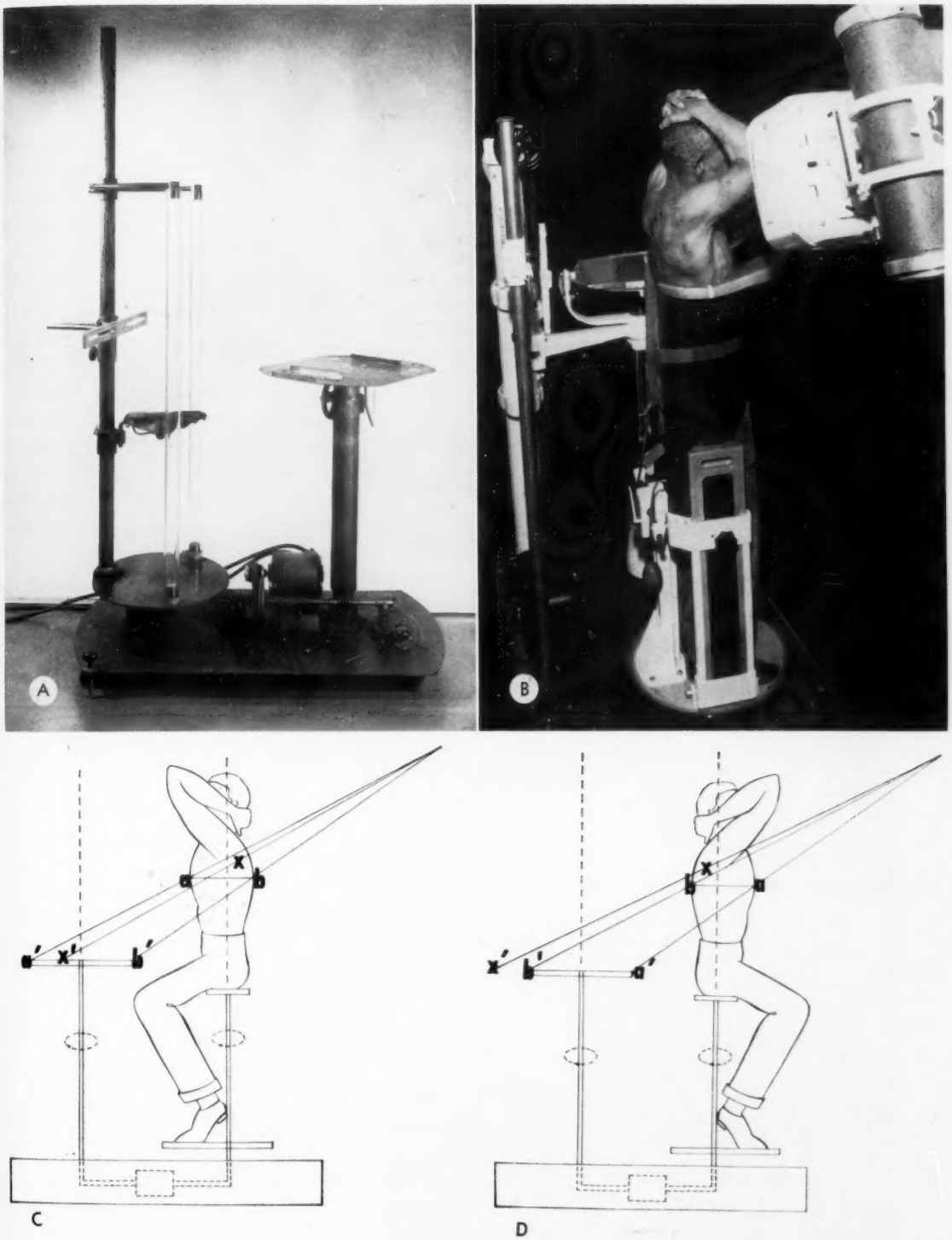

FIG. 3. (*A*) Original model of the first transverse laminagraphic equipment designed and utilized in this investigation. (*B*) Commercial model now employed in the Radiation Clinic. The roentgen tube housing carries a beam collimator and precisional light-localizing system. (*C*) Diagrammatic sketch illustrating principles of transverse laminagraphy. Points of all structures in selected plane (a–b) remain centered on identical points on the film (a′–b′), giving sharply defined stationary images. (*D*) After 180 degree rotation, the points of all structures situated outside the selected plane (X, for example) cast only moving shadows on or off the film and are therefore blurred or not reproduced.

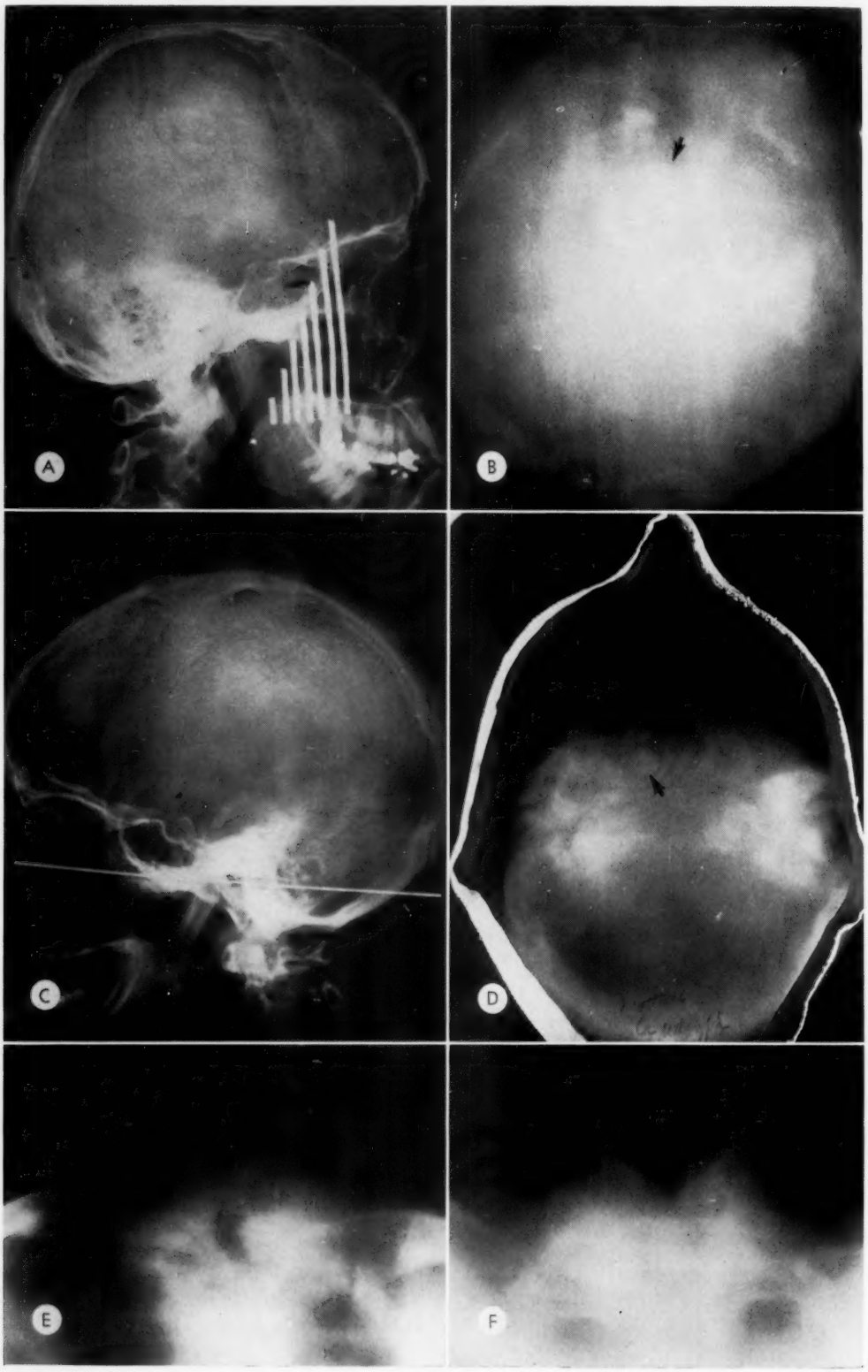

FIG. 4. (*A*) G. S., a white male thirty-three years of age with a recurrent nasopharyngeal tumor invading the sphenoid sinus after radiation therapy to the primary lesion and lymph nodes of the neck. The lead

utilized for routine roentgenography, this alignment is likely to be disturbed and may require daily checking and readjustment.

The patient must be positioned in the erect or sitting posture. Although the trunk is well immobilized by vertical stanchions and inflatable rubber bags, fixation of the head and neck is a far more difficult task. A special plastic rig is being fabricated to solve this problem, but for the present, a pair of huge sponge rubber blocks are used as wedges on each side of the head and neck.

The desired plane is indicated by a single pointer; the tube is focused with an optical device and light collimator; and the exposure is made by remote control during complete rotation. A typical exposure for the head requires 3.2 seconds, 110 ma. and 85 kv.; a typical exposure for the thorax demands 3.2 seconds, 110 ma. and 82 kv. By varying the angle of the tube head from 15° to 40°, the thickness of slice can be varied from 0.3 mm. to 1.3 mm. We have found an angle of 25° and a slice thickness of 0.5 mm. to be quite satisfactory.

At the outset, the radiation received by the patient during transverse laminagraphy was about three times that received from conventional roentgenography in the same anatomic area. Through the use of high speed film, developer and screens, the level of exposure has been materially reduced. For the cancer patient receiving roentgen therapy, this diagnostic irradiation is obviously of little significance. For the patient with a benign diagnostic problem, it becomes our responsibility to reduce the exposure to the minimum level consistent with a good roentgenographic result. The problem of radiation exposure, and other considerations as well, prompted us to design and fabricate an effective multifilm cassette for those situations demanding multiple slices in precisely parallel planes during a single exposure.

APPLICATION

After careful scrutiny of the patient's conventional roentgenograms and other diagnostic data, the principal transverse treatment plane is selected and a transverse laminagram is made. Our magnification factor of 1.38× appears to be reliable and constant. To reduce the roentgenographic images to life-size on a translucent paper planning sheet, one may employ a variety of devices such as a camera lucida, pantograph unit or proportional calipers. We prefer to copy the laminagram on a lantern slide, using the conventional or rapid Land method. The image is then projected in life-size upon the planning sheet by means of a photographic enlarger or lantern slide projector (Fig. 1*E*). The body contour, tumor and important normal structures may then be traced in with ease and accuracy (Fig. 1*F*). As a substitute for the photographic method, we have recently designed an optical system for instant reduction of the roentgenogram to a life-size image directly on the tracing panel. When the tumor is not well visualized, other localization studies are referred to, includ-

grid is a helpful marker for determining laminagraphic levels. (*B*) Transverse laminagram through the sphenoid sinus indicating massive invasion of this area. This cross-section served well in treatment planning with supervoltage roentgen therapy. (*C*) R.M., a forty-two year old white male with nasopharyngeal carcinoma, epidermoid type. The tumor was brought under control for several months with a dose of 6,000 r, but the patient returned with excruciating and unrelenting left parietal pain. Search for evidence of intracranial osseous invasion by conventional roentgenography was fruitless. (*D*) Transverse laminagram of the same patient through the pterygoid fossae shows obliteration of pterygoid bone on the left. This film designates the exact site of intracranial invasion, confirmed by needle biopsy. A small portal was arranged to cross-fire this site with additional irradiation and the patient was relieved of his distress. (*E*) H. K., a forty-two year old white male with a rapidly growing tracheal carcinoma. Laminagram for tumor localization shows large intraluminal lesion with marked distortion and displacement of the trachea. Extraluminal component of tumor is seen on the right, as well as massive pretracheal edema. (*F*) Transverse laminagram of the same patient after 6,000 r (tumor dose) shows restoration of normal contour of tracheal air shadow and disappearance of tumor mass.

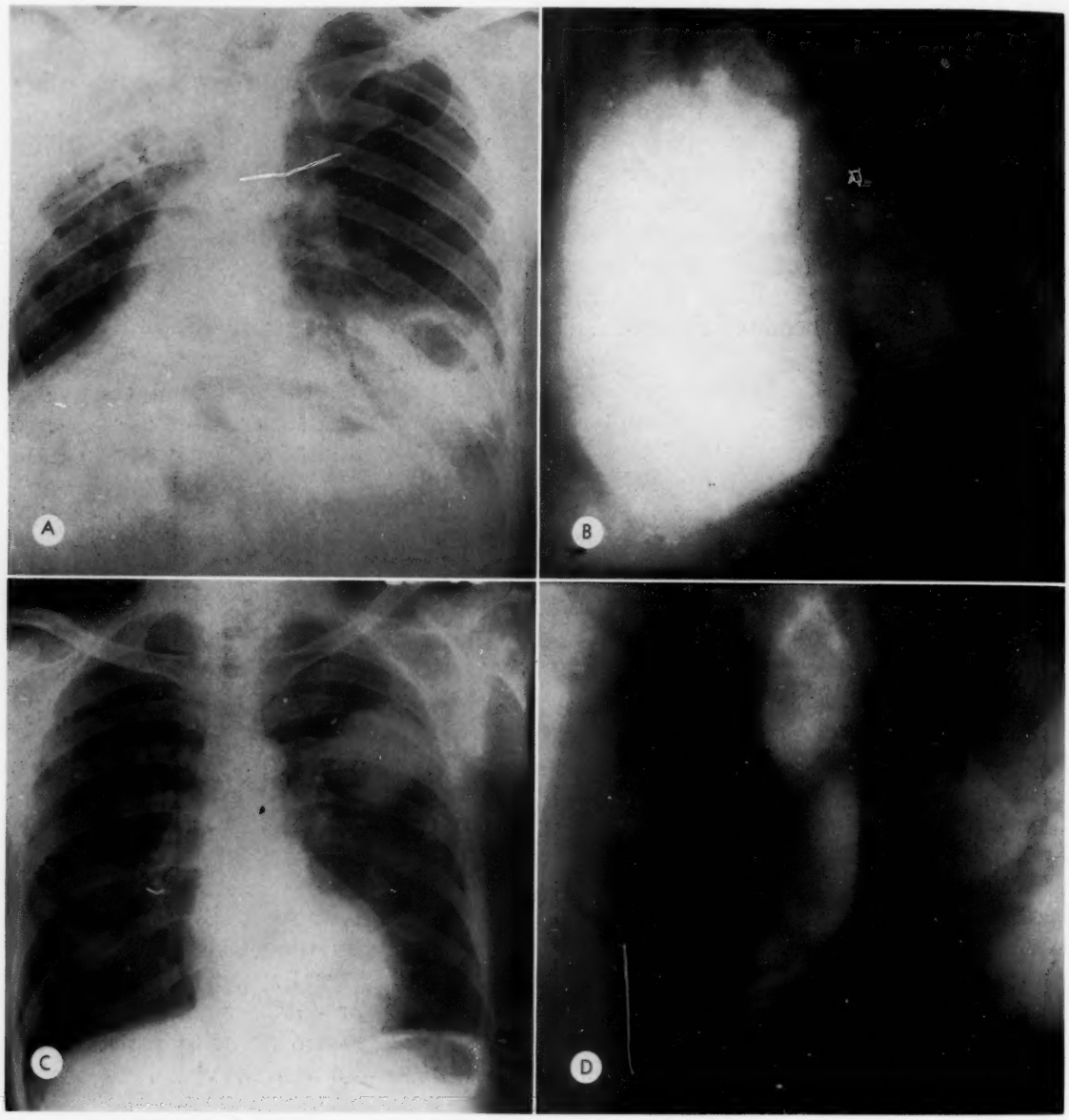

FIG. 5. (*A*) J.T., a thirty-eight year old white male with Hodgkin's disease of ten years' duration. Pulmonary lesion in the right upper lobe has remained controlled since 1951 after tumor dose of 4,000 r. Note large lesion at this time in left lower lobe, with cavitation. (*B*) Transverse laminagram of the same patient directly through the cavity, illustrating its thick and irregular walls suggesting malignant disease. Note especially the satellite infiltrates and lymph nodes contiguous to the principal lesion. Huge density on the right is the right lobe of the liver. Supervoltage roentgen therapy was directed to the cavitary lesion and lymph nodes, with complete resolution. (*C*) C.B., a sixty-five year old white male with expanding bronchogenic carcinoma of left upper lobe. Posteroanterior chest roentgenogram shows an apparently discrete peripheral lesion in the left lung. (*D*) Transverse laminagram of the same patient through the midline of lesion, at its greatest diameter, illustrates attachment to lateral chest wall. This finding was confirmed at thoracotomy. This laminagram would serve as an excellent basis for treatment planning, if the patient were to receive radical radiation therapy.

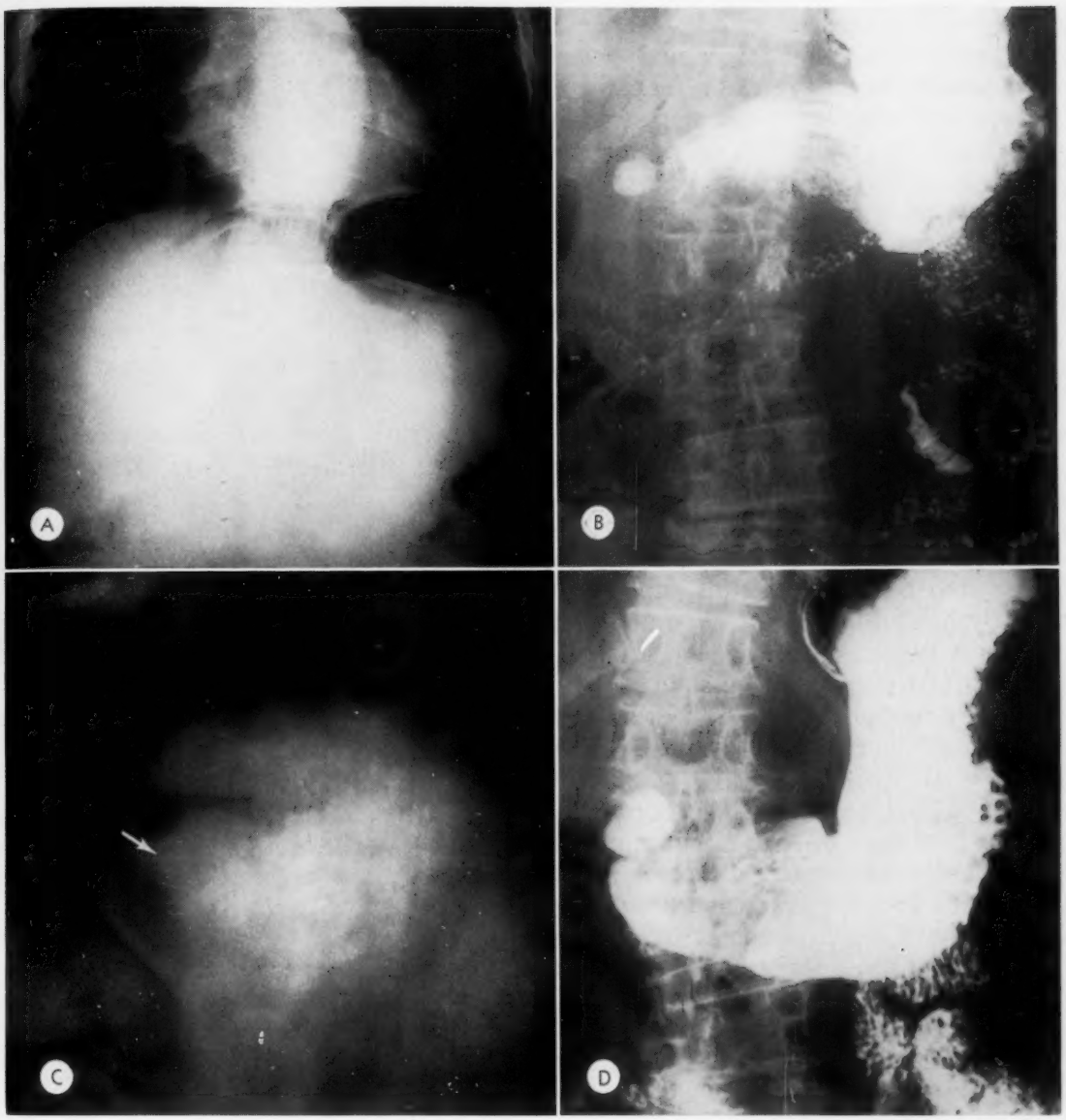

Fig. 6. (*A*) F.F., a sixty-four year old white male with lymphosarcoma involving the peripheral lymph nodes. Abdominal discomfort on the present admission was associated with some enlargement of the liver and spleen. The presence of a large para-aortic mass was noted by some examiners and denied by others. Posteroanterior chest roentgenogram shown here after pneumoperitoneum was not helpful. (*B*) Barium-filled stomach reveals an area of compression on the greater curvature consistent with the presence of a retroperitoneal mass in this area. (*C*) Transverse laminagram of same patient prior to therapy shows outline of enlarged liver and spleen, but especially the para-aortic mass of lymph nodes clearly displayed in relation to the gastric shadow. Pneumoperitoneum is of considerable value in this examination. (*D*) Barium-filled stomach after radiation therapy to the mass shows restoration of normal contour consistent with negative physical findings at this time and relief of abdominal discomfort.

ing tridimensional laminagraphy and the use of contrast media.

In the thorax and abdomen, it is not always possible to include all of the patient's transverse body section on the standard 14×14 inch film utilized in the commercial model. Modifications of the apparatus are therefore being made to permit a longer target-patient distance as well as introduction of a 14×17 inch cassette stand. In the meantime, the patient's complete body contour is obtained as usual at the selected level by means of a narrow strip of plaster bandage (resin-impregnated and fast-setting) and traced on the planning sheet (Fig. 1*B*). The image of the laminagram is then properly oriented within the traced contour (Fig. 1*E*).

It is in the head, neck and thorax that we have found transverse laminagraphy particularly helpful in defining the tumor volume as a prelude to treatment planning. Invasion of the base of the skull and the sinuses by nasopharyngeal and other neoplasms has been repeatedly and exquisitely demonstrated (Fig. 4, *A* and *B; C* and *D:* and *E* and *F*). Chest studies have often dissociated the core of dense tumor in the larger shadow of an atelectatic lobe in patients with bronchogenic carcinoma (Fig. 1*C*) and have aided in the elucidation of the nature of other lesions (Fig. 5, *A* and *B*). Frimann-Dahl[3] has stated that a tumor growing into the thoracic wall or the mediastinum may be detected by transverse laminagraphy, and more clearly so than by any other method. Our experience supports this observation (Fig. 5, *C* and *D*). For visualizing disease processes in the abdomen, retroperitoneal area and pelvis, it becomes necessary to inject a gas into the peritoneal cavity or the presacral space (Fig. 6, *A–D*).

Laminagrams of radium implants in the tongue and floor of the mouth (Fig. 7) suggest that horizontal laminagraphy with a multifilm cassette may prove of real value in three-dimensional reconstructions, dosage calculation and resident training.

Transverse laminagraphy has also proved helpful in following the progress of tumor regression during treatment and for evaluating the final result of radiation therapy in a more objective manner (Fig. 4, *E* and *F*).

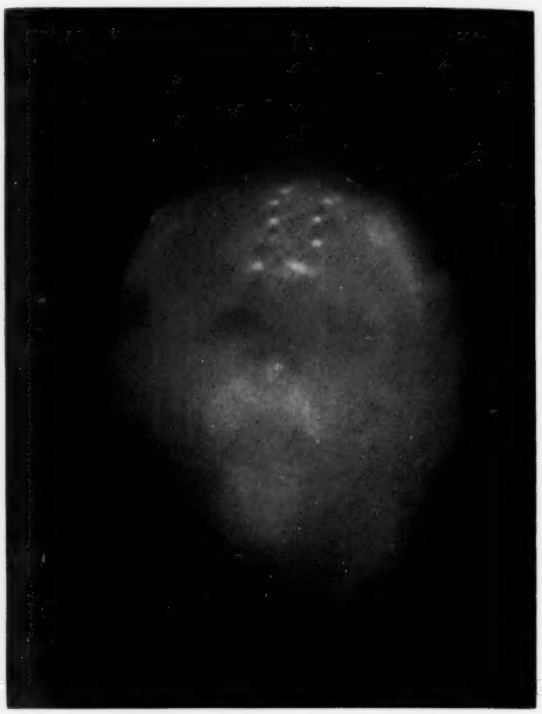

FIG. 7. J.O'M., a sixty-five year old patient with a large right lingual carcinoma treated by a two-plane radium implant. Transverse laminagram reveals the exact alignment of the needles at the midplane. Serial films in parallel planes through the use of a multifilm cassette provide an opportunity for graphic reconstruction of the actual implant and precise dosage calculation after the operation.

SUMMARY

1. In tumor localization and treatment planning for patients with deep seated cancer, it is necessary to construct an accurate graphic cross-section of the patient's body in the horizontal treatment plane, showing the body contour, the tumor volume and the correct spatial relationships of important normal structures.

2. The conventional technique for this purpose includes the use of roentgenograms and a standard anatomic cross-section atlas. There is nearly always a gross dis-

parity between the morbid anatomy of the sectioned cadaver (from which the atlas is drawn) and the living anatomy of the cancer patient. Furthermore, conventional roentgenograms are not always helpful in delineating the volumetric limits of the malignant lesion.

3. Transverse laminagraphy provides a living anatomic cross-section of the patient under consideration as a sound basis for tumor localization, portal selection, beam orientation, isodose plotting and dosage distribution. On the success of this effort may depend, in large measure, the patient's chance for cure, as well as the fate of normal structures in the path of the beam.

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REFERENCES

1. Amisano, P. Three dimensional stratigraphic examination; axial transverse stratigraphy. Part II. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1955, *74*, 777–790.
2. Frain, C., and Lacroix, F. Courbe-enveloppe et coupes horizontales. *J. de radiol. et d'électrol.*, 1947, *28*, 142–143.
3. Frimann-Dahl, J. Tomography, bronchography and angiography in study of bronchial carcinomas. Estratta da: Stratigrafia-Planigraphie-Tomographie-Laminagraphy-Estratigrafia, 1956, Vol. I, No. 1, 25–32.
4. Gebauer, A. Körperschichtaufnahmen in transversalen (horizontalen) Ebenen. *Fortschr. a. d. Geb. d. Röntgenstrahlen ver. m. Röntgenpraxis*, 1949, *71*, 669–696.
5. Gebauer, A., and Wachsmann, F. Geometrische Betrachtungen und technische Fragen zur Herstellung transversaler Körperschichtaufnahmen. *Röntgen Blätter*, 1949, *5*, 215–229.
6. Gebauer, A. Körperschichtaufnahmen in transversalen Ebenen. *Tuberkulosearzt*, 1951, *5*, 151–156.
7. Gebauer, A. Diagnostische Vorteile und Indikationsstellung der Körperschichtaufnahmen in transversalen Ebenen gegenüber denen in vertikalen. *Fortschr. a. d. Geb. d. Röntgenstrahlen*, 1951, *75*, 9–21.
8. Gebauer, A., and Schanen, A. Das transversale Schichtverfahren. *Fortschr. a. d. Geb. d. Röntgenstrahlen ver. m. Röntgenpraxis*, 1955, Ergänzungsband 71, pp. 1–313.
9. Gebauer, A., and Schanen, A. Das transversale Schichtverfahren. Georg Thieme, Stuttgart, Germany, 1955.
10. Roswit, B., Unger, S. M., Stein, J., Malsky, S. J., and Reid, C. Transverse tomography—third dimension in body section roentgenography. Exhibit presented at the Fifty-eighth Annual Meeting of the American Roentgen Ray Society, Washington, D. C., October 1–4, 1957.
11. Roswit, B., Unger, S. M., Stein, J., Malsky, S. J., and Reid, C. Horizontal body section radiography. Presented at the Eastern Conference of Radiologists, New York, New York, March, 1957.
12. Stevenson, J. J. Horizontal body section radiography. *Brit. J. Radiol.*, 1950, *23*, 319–334.
13. Vallebona, A. I nuovi orizzonti della stratigrafia nei vari campi della medicina; l'esplorazione stratigrafica tridimensionale. *Inform. med., Genova*, 1948, *22*, 89–96.
14. Vallebona, A. I nuovi orizzonti della stratigrafia nei vari campi della medicina. Estratta da: *Inform. med., Genova*. Sez. Clinico Scientifica, 1948, I, fasc. 4.
15. Vallebona, A. Three dimensional stratigraphic examination; axial transverse stratigraphy. Part I. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1955, *74*, 769–776.
16. Watson, W. Differential radiography. *Radiography*, 1939, *5*, 81–88; also, 1940, *6*, 161–172.
17. Watson, W. Differential radiography; body-section radiography in practice. *Radiography*, 1943, *9*, 33–38.
18. Watson, W. British Patent 508,381, December, 1937; U. S. Patent 293,720, December, 1937.

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Sixtieth Annual Meeting: Netherland-Hilton Hotel, Cincinnati, Ohio, September 22–25, 1959.

AMERICAN RADIUM SOCIETY

President: Milford D. Schulz, Boston, Mass.; *President-Elect:* Theodore R. Miller, New York, N. Y.; *1st Vice-President:* Theodore P. Eberhard, Ann Arbor, Mich.; *2nd Vice-President:* James F Nolan, Los Angeles, Calif.; *Secretary:* Robert L. Brown, P. O. Box 459, Emory University, Atlanta 22, Ga.; *Treasurer:* Jesshill Love, 234 Medical Arts Bldg., 1169 Eastern Parkway, Louisville, Ky.

Executive Committee: Grant H. Beckstrand, Chairman, Long Beach, Calif.; Norman A. McCormick, Windsor, Ontario, Canada; Ralph T. Ogden, Hartford, Conn.

Program Committee: Milford D. Schulz, Chairman, Boston, Mass.; Lloyd F. Craver, New York, N. Y.; Morton M. Kligerman, New York, N. Y.; Elizabeth F. Focht, New York, N. Y.; J. Samuel Binkley, Oklahoma City, Okla.; Justin J. Stein, Los Angeles, Calif.; William S. MacComb, Houston, Texas; Theodore R. Miller (ex officio), New York, N. Y.

Publication Committee: Harry Hauser, Chairman, Cleveland, Ohio; Martin Van Herik, Rochester, Minn.; J. Robert Andrews, Bethesda, Md.

Public Relations Committee: Henri LeClaire, Chairman, Cincinnati, Ohio; John V. Blady, Philadelphia, Pa.; Harold E. Johns, Toronto, Ontario, Canada.

Janeway Lecture Committee: Gioacchino Failla, Chairman, New York, N. Y.; H. Dabney Kerr, St. Michaels, Md.; Lloyd F. Craver, New York, N. Y.

Representatives on the American Board of Radiology: Douglas Quick, New York, N. Y.; B. P. Widmann, Philadelphia, Pa.; Frederick W. O'Brien, Boston, Mass.

Representatives on the National Committee on Radiation Protection: Edith H. Quimby, New York, N. Y.; Theodore P. Eberhard, Ann Arbor, Mich.

Representative on the Board of Chancellors of the American College of Radiology: Charles L. Martin, Dallas, Texas.

Committee on Arrangements: Charles C. Stetson, Chairman, Englewood, N. J.; Henri LeClaire, Cincinnati, Ohio; Victor A. Marcial, Puerto Rico; Howard H. Ashbury, Charlottesville, Va.; Jesshill Love, Louisville, Ky.

Forty-first Annual Meeting: The Homestead, Hot Springs, Virginia, April 6–8, 1959.

EDITORIALS

THE FORTY-FIRST ANNUAL MEETING OF THE AMERICAN RADIUM SOCIETY

NINETEEN hundred and fifty-nine is the sixtieth complete year since the Curies made the element radium known to the world; it is the twenty-fifth year in the age of artificial radioactivity initiated by the daughter of the Curies—Irene, and her husband, F. Joliot; it is the forty-third year of the American Radium Society and the year of its Forty-first Annual Meeting.

This meeting will occur at the Homestead in Hot Springs, Virginia, on Monday, Tuesday, and Wednesday, the sixth, seventh, and eighth of April.

All physicians and allied scientists interested in the management of malignant disease, especially its management by ionizing radiation, and those interested in the basic physical and biologic aspects of ionizing radiation, are invited to attend.

The American Radium Society has as its stated purpose the promotion of "the scientific study of radium and other sources of ionizing radiation in relation to their physical properties and their therapeutic applications." It is, so to speak, of two souls, each dependent on the other; the one concerned with the fundamental physical and biologic aspects of ionizing radiation, and the other concerned with the use of these ionizing radiations in the healing of the sick, especially those sick of malignant neoplastic diseases, and, in a wider sense, concerned with the management of malignant neoplastic diseases in general.

The scientific program, a tentative and preliminary schedule of which appears elsewhere in this issue of the JOURNAL, was conceived with these objectives in mind. The papers and symposia, though a moratorium is observed in several areas which have been intensively examined in recent meetings of the society, are of general interest and will be presented at three continuous, somewhat extended, morning sessions, leaving the time after lunch for informal discussions, the showing of scientific cinema, and other unscheduled events. It has long been felt by many that a most important reason for attending a scientific meeting was that it gave those doing similar work an opportunity to discuss problems and exchange ideas. It is hoped that by leaving time after lunch free of formally scheduled sessions this need will be filled.

Special mention should be made of one day's program which has to do with the general theme, "Why do not things in cancer management always go as intended and what do we do then?" It seems well to occasionally examine both sides of the coin.

There will be no discussions of individual papers. All discussions will be postponed until the end of each scientific session where time is set aside. It is hoped that active and general discussion from the floor will be stimulated by appropriate abettors.

The Janeway Lecture, always an outstanding occasion, will occur late in the afternoon on Monday. The Janeway Committee has chosen as the twenty-fourth medalist and lecturer one of this Society's most remarkable members, Dr. James T. Case. Dr. Case is one of the two surviving Charter Members of the American Radium Society; he was its eighth president; and he was the second editor of this, the official JOURNAL of the Society. His lecture cannot help but be of the first order.

The American Radium Society has always been recognized as a most pleasant organization, the social as well as the scientific events looked forward to with antici-

pation and back upon with pleasure. Your Committee on Arrangements has been very active, and it has been anticipated that this year shall be no exception. On Monday evening immediately after the Janeway Lecture, the Society and its nonmember registrants are to be the guests of the Radium Chemical Company at a social hour. An informal dinner and dancing ad libitum then will follow. On the second evening the regular reception for members and guests of the Society will be followed by the Annual Banquet and presentation of the Janeway Medal. Entertainment of a new sort is promised by the Arrangements Committee.

The facilities of the Homestead offer varied opportunities for entertainment, but particular attention has been given to the social program of the lady guests who will accompany those occupied with more serious matters so that their stay may be more enjoyable.

The Homestead is a delightful hotel with an atmosphere of relaxation and gracious living rarely found nowadays. Removed from the hustle and bustle of a large convention city and of the usual tourist-occupied resort, it is a delight and in the spring, when the dogwoods of its seventeen thousand acres of woodland are in bloom, it should be most pleasant.

In addition to its famed spa, a wide variety of activities are offered by the hotel—riding, hiking, golfing, shooting and fishing in season, to mention a few, or just plain loafing and relaxing. It operates on the American plan. The Homestead is located in the mountains of western Virginia on U. S. Route 220 between U. S. Route 60 and U. S. Route 39. It is most conveniently reached by auto or rail. Through overnight Pullman service is provided daily from Washington, Baltimore, Philadelphia, and New York by the C. & O. Railroad. Persons arriving from the West will detrain at Covington, Virginia, where transportation by bus to the Homestead is provided without additional charge if through tickets to Hot Springs are purchased. Those desiring to travel by air will find service to Roanoke, Virginia, provided by Eastern, American, and Piedmont Airlines from whence air taxi, limousine, or hire auto may be taken.

Registration will commence on Sunday, the fifth of April, but advance registration is encouraged and should be made with Dr. Charles Stetson at Englewood Hospital, 350 Engle Street, Englewood, New Jersey. Reservations at the hotel can be made directly with the management. No doubt, many will wish to take advantage of the occasion and extend their stay beyond the dates of the meeting. Special note should be made of this intent when making reservations.

Again, the officers of the American Radium Society invite you to its Forty-first Annual Meeting: to meet old friends and to make new; to relax and enjoy a respite from the day's toil; and to learn and to help others to learn.

MILFORD D. SCHULZ, M.D., *President*
The American Radium Society

Massachusetts General Hospital
Boston 14, Massachusetts

ADONIRAM JUDSON QUIMBY
1875–1958

ADONIRAM JUDSON QUIMBY died on August 24, 1958, in St. Barnabas' Hospital, New York, following a stroke which left him disabled for eight and one-half years.

Dr. Quimby was born April 4, 1875, in Wheeling, West Virginia, and followed-up his public-school education with courses in chemistry at the Lindsay Institute there. He obtained a degree in pharmacy from the Ohio Medical College in Columbus in 1898 and his M.D. in 1905. He then established an x-ray laboratory in Wheeling. In 1910 he moved to New York. Dr. Wyeth, Chief Surgeon of the Polyclinic Hospital, requested that he establish and conduct an

X-ray Department there, which he did. He resigned in 1916 and in 1923 returned to the hospital as Professor of Roentgenology and Director of the Department. At the beginning, only one room was available for the X-ray Department. In 1934 the Department was re-equipped, and when Dr. Quimby left in 1936 it had grown to five rooms.

Dr. Quimby was Assistant Radiologist and Lecturer in the X-ray Department of the New York Post-graduate Hospital from 1910 to 1912. At the same time he was Visiting Roentgenologist and Electrotherapist of the New York Throat, Nose and Lung Hospital, and Assistant to the Roentgenologist of the New York Hospital for the Ruptured and Crippled. From 1912 to 1924 he was Visiting Roentgenologist of the New York Foundling Hospital. From 1914 to 1921 he was Visiting Roentgenologist of the Central Neurological Hospital on Blackwells Island. He was also Visiting Roentgenologist of the Flower Hospital, of St. Mary's Hospital, St. Francis Hospital, and of a number of other hospitals.

He contributed numerous articles to the literature of his specialty; his interest was particularly engaged in protection against radiation, intestinal stasis, the gallbladder, the thyroid and the thymus.

The devotion of his wife Gertrude, to whom he was married in 1910, never faltered during his long last illness, when he was too ill to have any other visitors. He is survived also by a sister, Mrs. Mary Kennedy, three brothers, Dr. Will Quimby of Wheeling, West Virginia, and John and Charles; and a daughter, Mrs. Alice Dungan. His membership in the American Roentgen Ray Society dates back to 1910.

RAMSAY SPILLMAN, M.D.

NATIONAL COMMITTEE ON RADIATION PROTECTION AND MEASUREMENTS (NCRP)

SUPPLEMENT TO RADIATION HANDBOOKS SUMMARIZES NEW RECOMMENDATIONS ON MAXIMUM PERMISSIBLE DOSE

AN 8-page supplement to the National Bureau of Standards Handbooks[1] dealing with radiation protection and related matters has been prepared by the National Committee on Radiation Protection and Measurements (NCRP). Entitled *Maximum Permissible Radiation Exposures for Man*, the supplement summarizes the new recommendations of the NCRP on safe limits of radiation exposure; it extends and clarifies the Preliminary Statement issued by the Committee in January 1957.[2] The new publication introduces only minor changes and is intended to be in general conformity with the philosophy expressed in the April, 1956 statements of the International Commission on Radiological Protection (ICRP).[3]

The recommendations of the NCRP, an advisory group of experts in various phases of the radiation field, are regularly published in the NBS Handbooks series. Several of these Handbooks are now being revised to bring them into conformity with the new recommendations. Pending the availability of the revised Handbooks, the present supplement provides a simplified statement of the changes needed to comply with the new recommendations.

Further details on the new supplement are given in the following excerpts from its introduction.

Excerpts from NCRP Statement

On January 8, 1957 the National Committee on Radiation Protection and Measurements issued a Preliminary Statement setting forth its revised philosophy on Maximum Permissible Radiation Exposures to Man.[2] Since that time, several of the NCRP subcommittees have been actively studying the necessary revisions of their respective Handbooks. These studies have shown the need for (1) clarification of the earlier statement and (2) modification or extension of some of the concepts in that statement. Furthermore, the ICRP has made minor changes in their recommendations. Accordingly, the NCRP has prepared a set of guides, given below, that will assure uniformity in the basic philosophy to be embodied in the several Handbooks. Since many of the Handbooks are followed closely in planning radiation operations in the United States, and since the modification of a Handbook may require many months of effort, it seems wise to make the overall guiding principles available in advance of the reissuance of the revised Handbooks. These guides are not designed to take the place of any of the Handbooks; the principles given below will be extensively treated later in appropriate places. In the meantime, Handbook revisions or supplementary statements will be issued as rapidly as possible. . . .

The changes in the accumulated MPD (Maximum Permissible Dose) are not the result of positive evidence of damage due to use of the earlier permissible dose levels, but rather are based on the desire to bring the MPD into ac-

[1] *The supplement is being supplied with the following NBS Handbooks:* H42, Safe handling of radioactive isotopes (20¢); H48, Control and removal of radioactive contamination in laboratories (15¢); H49, Recommendations for waste disposal of phosphorus-32 and iodine-131 for medical users (15¢); H51, Radiological monitoring methods and instruments (20¢); H50, X-ray protection (20¢); H52, Maximum permissible amounts of radioisotopes in the human body and maximum permissible concentrations in air and water (25¢); H53, Recommendations for the disposal of carbon-14 wastes (15¢); H54, Protection against radiations from radium, cobalt-60, and cesium-137 (25¢); H55, Protection against betatron-synchrotron radiations up to 100 million electron volts (25¢); H56, Safe handling of cadavers containing radioactive isotopes (15¢); [*Note: H56 has been superseded by H65, Safe handling of bodies containing radioactive isotopes* (15¢); *H65 embodies all recent changes and does not need the supplement*]; H58, Radioactive-waste disposal in the ocean (20¢); H59, Permissible dose from external sources of ionizing radiation (30¢); H60, X-ray protection (20¢); H61, Regulation of radiation exposure by legislative means (25¢). *These Handbooks are available at the indicated prices per copy from the Superintendent of Documents, U. S. Government Printing Office, Washington 25, D. C.*

Present holders of the above Handbooks can secure copies of the supplement by writing to the Publications Section National Bureau of Standards, Washington 25, D. C.

[2] Maximum permissible radiation exposures to man, *NBS Tech. News Bul. 41, 17 (Feb. 1957)*; *Radiology*, 1957, *68*, 260; Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1957, *77*, 910.

[3] Report on 1956 amendments to the recommendations of the International Commission on Radiological Protection (ICRP), *Radiology, 70, 261 (Feb. 1958)*.

cord with the trends of scientific opinion; it is recognized that there are still many uncertainties in the available data and information. Consideration has also been given to the probability of a large future increase in radiation uses. In spite of the trends, it is believed that the risk involved in delaying the activation of these recommendations is very small if not negligible. Conditions in existing installations should be modified to meet the new recommendations as soon as practicable, and the new MPD limits should be used in the design and planning of future apparatus and installations. Because of the impact of these changes and the time required to modify existing equipment and installations, it is recommended on the basis of present knowledge that a conversion period of not more than 5 years from January, 1957 be adopted, within which time all necessary modifications should be completed.

SOCIETY PROCEEDINGS AND NEWS ITEMS

MEETINGS OF RADIOLOGICAL SOCIETIES*

United States of America

American Roentgen Ray Society
Secretary, Dr. C. Allen Good, Mayo Clinic, Rochester, Minn. Annual meeting: Netherland-Hilton Hotel, Cincinnati, Ohio, Sept. 22–25, 1959.

American Radium Society
Secretary, Dr. Robert L. Brown, P.O. Box 459, Emory University, Ga. Annual meeting: The Homestead, Hot Springs, Va., April 6–8, 1959.

Radiological Society of North America
Secretary, Dr. D. S. Childs, 713 E. Genesee St., Syracuse 2, N. Y. Annual meeting: Palmer House, Chicago, Ill., Nov. 16–21, 1958.

American College of Radiology
Executive Director, William C. Stronach, 20 N. Wacker Drive, Chicago 6, Illinois. Annual meeting: Feb. 4–7, 1959, Chicago, Ill.

Section on Radiology, American Medical Association
Secretary, Dr. T. Leucutia, Harper Hospital, Detroit 1, Mich. Annual meeting: June 8–12, 1959, Atlantic City, N. J.

American Board of Radiology
Secretary, Dr. H. Dabney Kerr. Correspondence should be directed to Kahler Hotel Building, Rochester, Minn. Special Spring Examination, March 16–19, 1959, Cincinnati, Ohio; deadline for filing applications was November 1, 1958. Candidates completing training June 30, 1959 are not eligible for the Spring 1959 examination.

Ninth International Congress of Radiology
Secretary-General, Dr. Hans v. Braunbehrens. Request for information should be addressed to Dr. Viktor Loeck, Kongressbüro, Forsthausstrasse 76, Frankfurt am Main, Germany. Meets in Munich, Germany, July 23 to July 30, 1959.

Seventh Inter-American Congress of Radiology
Secretary, Dr. Laura Fariñas, Havana, Cuba. *Counselor for the United States*, Dr. J. A. del Regato, Penrose Cancer Hospital, 2200 North Cascade Avenue, Colorado Springs, Colorado. The meeting will be held in Brazil in 1961.

Alabama Radiological Society
Secretary, Dr. J. A. Meadows, Jr., Medical Arts Bldg., Birmingham 5, Ala. Meets time and place Alabama State Medical Association.

American Nuclear Society
Executive-Secretary, Octave J. Du Temple, 86 E. Randolph St., Chicago, Ill.

Arizona Radiological Society
Secretary, Dr. R. Lee Foster, 1313 N. Second St., Phoenix, Ariz. Two regular meetings a year. Annual meeting at time and place of State Medical Association and interim meeting six months later.

Arkansas Radiological Society
Secretary, Dr. E. A. Mendelsohn, Holt-Krock Clinic, Fort Smith, Ark. Meets every three months and also at time and place of State Medical Association.

Association of University Radiologists
Secretary, Dr. Paul Riemenschneider, Medical College. State University of New York, Syracuse, N. Y. Annual meeting: Spring, 1959 in Atlanta, Ga.

Atlanta Radiological Society
Secretary, Dr. J. L. Clements, Jr., 35 Linden Ave., N.E., Atlanta 8, Ga. Meets monthly, except during three summer months, on second Friday evening.

Blockly Radiological Society
Secretary, Dr. Samuel Finkelman, 101 S. Twentieth St. Philadelphia, Pa.

Brooklyn Radiological Society
Secretary, Dr. George A. Manfredonia, One Hanson Place, Brooklyn, N. Y. Meets first Thursday of each month October through May.

Buffalo Radiological Society
Secretary, Dr. Alfred Dobrak, 710 Leydecker Rd., Buffalo 24, N. Y. Meets second Monday evening each month, October to May inclusive.

Central New York Roentgen Ray Society
Secretary, Dr. Joseph A. Head, 150 Marshall St., Syracuse, N. Y. Meets first Monday each month October through May.

Central Ohio Radiological Society
Secretary, Dr. Arthur R. Cohen, 41 S. Grant Ave., Columbus, Ohio. Meets at 6:30 P.M. on second Thursday of October, November, January, March and May at Fort Hayes Hotel, Columbus, Ohio.

Central Society of Nuclear Medicine
Secretary, Dr. Robert S. Landauer, Radiation Center Building, 1903 West Harrison St., Chicago 12, Ill.

Chicago Roentgen Society
Secretary, Dr. George B. Cahill, 802 Burns Ave., Flossmoor, Ill. Meets second Thursday of each month, October to April except December at the Sheraton Hotel at 8:00 P.M.

Cleveland Radiological Society
Secretary, Dr. Frederick A. Rose, 2065 Adelbert Rd., Cleveland 6, Ohio. Meetings at 7:00 P.M. on fourth Monday of each month from October to April at Tudor Arms Hotel.

Colorado Radiological Society
Secretary, Dr. Lorenz R. Wurtzebach, 601 E. Nineteenth Ave., Denver, Colo. Meets third Friday of each month at Denver Athletic Club.

Connecticut Valley Radiologic Society
Secretary, Dr. Paul J. Kingston, 114 Woodland St., Hartford, Conn. Meets first Friday in February and April.

Dallas-Fort Worth Radiological Club
Secretary, Dr. A. H. Keene, 3707 Gaston Ave., Dallas, Texas. Meets monthly, third Monday, at Greater Fort Worth International Airport at 6:30 P.M.

Detroit Roentgen Ray and Radium Society
Secretary, Dr. Joseph O. Reed, Jr., Harper Hospital, Detroit 1, Mich. Meets monthly first Thursday, October through May, at David Whitney House, 1010 Antietam, at 6:30 P.M.

East Bay Roentgen Society
Secretary, Dr. Dan Tucker, 434 30th St., Oakland 9, Calif. Meets first Thursday each month at Peralta Hospital, Oakland.

East Tennessee Radiological Society
Secretary, Dr. Charles W. Reavis, Baroness Erlanger Hospital, Chattanooga, Tenn. Meets in January and September.

Eastern Radiological Society
Secretary, Dr. John D. Osmond, Jr., Euclid-Glenville Hospital, Cleveland 19, Ohio.

Florida Radiological Society
Secretary, Dr. Russell D. D. Hoover, 49th St., West

*** Secretaries of societies are requested to send timely information promptly to the Editor.**

Palm Beach, Fla. Meets twice annually, in the spring with the annual State Society meeting, and in the fall.

GEORGIA RADIOLOGICAL SOCIETY
Secretary, Dr. B. H. Malone, 1406 Reynolds St., Brunswick, Ga. Meets Spring and Fall with Annual State Society Meeting.

GREATER MIAMI RADIOLOGICAL SOCIETY
Secretary, Dr. George P. Daurelle, Jackson Memorial Hospital, Miami 36, Fla. Meets monthly third Wednesday at 8 P.M. at Jackson Memorial Hospital, Miami, Fla.

GREATER ST. LOUIS RADIOLOGICAL SOCIETY
Secretary, Dr. Charles J. Cherre, 462 N. Taylor, St. Louis 8, Mo.

HOUSTON RADIOLOGICAL SOCIETY
Secretary, Dr. Edward B. Singleton, 6621 Fannin St., Houston 25, Texas. Meets last Monday each month, Seminar Room, Doctors' Club of Houston.

IDAHO STATE RADIOLOGICAL SOCIETY
Secretary, Dr. Charles R. McWilliams, Magic Valley Memorial Hospital, Twin Falls, Idaho. Meets annually at same time as Idaho State Medical Association.

ILLINOIS RADIOLOGICAL SOCIETY
Secretary, Dr. Stephen L. Casper, 1101 Maine St., Quincy, Ill. Meets three times a year.

INDIANA ROENTGEN SOCIETY
Secretary, Dr. C. A. Stayton, Jr., 313 Hume-Mansur Bldg., Indianapolis 4, Ind. Meets first Sunday in May and during fall meeting of Indiana State Medical Association.

IOWA RADIOLOGICAL SOCIETY
Secretary, Dr. James T. McMillan, 1104 Bankers Trust Bldg., Des Moines, Iowa. Luncheon and business meeting during annual session of Iowa State Medical Society. The scientific section is held in the autumn.

KANSAS RADIOLOGICAL SOCIETY
Secretary, Dr. James R. Stark, 3244 E. Douglas, Wichita, Kansas. Meets in spring with State Medical Society, and in winter on call.

KENTUCKY RADIOLOGICAL SOCIETY
Secretary, Dr. Robert H. Akers, 1405 West Broadway, Louisville 3, Ky. Meets monthly on second Friday at Seelbach Hotel, Louisville.

KINGS COUNTY RADIOLOGICAL SOCIETY
Secretary, Dr. C. P. Naidorf, 411 Parkside Ave. Brooklyn 26, N. Y. Meets Kings County Med. Soc. Bldg. monthly on fourth Thursday, October to May, 8:45 P.M.

LOS ANGELES RADIOLOGICAL SOCIETY
Secretary, Dr. Robert B. Engle, St. Luke Hospital, Pasadena, Calif. Meets second Wednesday of month in September, November, March, April and June at Los Angeles County Medical Association Building, Los Angeles.

MAINE RADIOLOGICAL SOCIETY
Secretary, Dr. Francis J. O'Connor, Augusta General Hospital, Augusta, Maine. Meets in June, September, December and March.

MARYLAND RADIOLOGICAL SOCIETY
Secretary, Dr. Nathan B. Hyman, 1805 Eutaw Place, Baltimore 17, Md.

MEMPHIS ROENTGEN SOCIETY
Secretary, Dr. James L. Booth, 899 Madison Ave., Memphis 3, Tenn. Meets first Monday of each month at John Gaston Hospital.

MIAMI VALLEY RADIOLOGICAL SOCIETY
Secretary, Dr. S. F. Johnson, 2197 Los Arrow Dr., Dayton 9, Ohio. Meets second Friday of fall and winter months.

MID-HUDSON RADIOLOGICAL SOCIETY
Secretary, Dr. Joseph Sorrentino, St. Francis Hospital, Poughkeepsie, N. Y. Meets 8:30 P.M., fourth Wednesday each month, September to May.

MILWAUKEE ROENTGEN RAY SOCIETY
Secretary, Dr. Joseph F. Wepfer, 5000 W. Chambers St., Milwaukee 10, Wis. Meets monthly on fourth Monday at University Club.

MINNESOTA RADIOLOGICAL SOCIETY
Secretary, Dr. Donald H. Peterson, 853 Medical Arts Bldg., Minneapolis 2, Minn. Meets three times annually, in fall, winter and spring.

MISSISSIPPI RADIOLOGICAL SOCIETY
Secretary, Dr. Robert P. Henderson, 316 Medical Arts Bldg., Jackson, Miss. Meets third Thursday of each month at Hotel Edwards, Jackson, at 6:00 P.M.

MONTANA RADIOLOGICAL SOCIETY
Secretary, Dr. Arthur T. Austin, 104 The Doctors Bldg., Billings, Montana. Meets at least once a year.

NASSAU RADIOLOGICAL SOCIETY
Secretary, Dr. Jerome Zwanger, 126 Hicksville Rd., Massapequa, L. I., N. Y. Meets second Tuesday of the month in February, April, June, October and December.

NEBRASKA RADIOLOGICAL SOCIETY
Secretary, Dr. J. F. Kelly, Jr., 816 Medical Arts Bldg., Omaha, Neb. Meets third Wednesday of each month at 6 P.M. in Omaha or Lincoln.

NEW ENGLAND ROENTGEN RAY SOCIETY
Secretary, Dr. John E. Gary, 1180 Beacon St., Brookline 46, Mass. Meets third Friday of each month, October through May, at The Longwood Towers, Brookline, Mass.

NEW HAMPSHIRE ROENTGEN RAY SOCIETY
Secretary, Dr. Paul Y. Hasserjian, 1470 Elm St., Manchester, N. H. Meets four to six times yearly.

NEW YORK ROENTGEN SOCIETY
Secretary, Dr. Harold G. Jacobson, 210th St. and Bainbridge Ave., New York 67, N. Y. Meets monthly on third Monday, New York Academy of Medicine, at 4:30 P.M.

NORTH CAROLINA RADIOLOGICAL SOCIETY
Secretary, Dr. William H. Sprunt, North Carolina Memorial Hospital, Chapel Hill, N. C. Meets in May and October.

NORTH DAKOTA RADIOLOGICAL SOCIETY
Secretary, Dr. Marianne Wallis, St. Joseph's Hospital, Minot, N D. Meetings by announcement.

NORTH FLORIDA RADIOLOGICAL SOCIETY
Secretary, Dr. Marvin Harlan Johnston, Five Points Medical Center, Jacksonville 4, Fla. Meets quarterly in March, June, September and December.

NORTHEASTERN NEW YORK RADIOLOGICAL SOCIETY
Secretary, Dr. Irving Van Woert, Jr., Albany Hospital, Albany, N. Y. Meets in Albany area on second Wednesday of October, November, March and April.

NORTHERN CALIFORNIA RADIOLOGICAL SOCIETY
Secretary, Dr. Rob H. Kirkpatrick, 1219 28th St., Sacramento, Calif. Meets at dinner last Monday of each month, September to June.

OHIO STATE RADIOLOGICAL SOCIETY
Secretary, Dr. Francis C. Curtzwiler, 421 Michigan St., Toledo 2, Ohio. Annual meeting: Cincinnati, Ohio, May, 1959.

OKLAHOMA STATE RADIOLOGICAL SOCIETY
Secretary, Dr. Edmond H. Kalmon, Jr., 300 Northwest 12th Street, Oklahoma City, Okla. Three regular meetings annually.

OREGON RADIOLOGICAL SOCIETY
Secretary, Dr. C. V. Allen, Veterans Hospital, Portland, Ore. Meets monthly from October to June on the second Wednesday of each month at 8:00 P.M. at the University Club.

ORLEANS PARISH RADIOLOGICAL SOCIETY
Secretary, Dr. Joseph V. Schlosser, Charity Hospital, New Orleans 13, La. Meets second Tuesday of each month.

PACIFIC NORTHWEST RADIOLOGICAL SOCIETY
Secretary, Dr. J. Arch Colburn, 19 Royal Oak Drive, Roseburg, Ore. Meets annually in May.

PACIFIC ROENTGEN SOCIETY
Secretary, Dr. L. H. Garland, 450 Sutter St., San Francisco 8, Calif. Meets annually during meeting of California Medical Association.

Pennsylvania Radiological Society
Secretary, Dr. Walter P. Bitner, 234 State St., Harrisburg, Pa. Annual meeting: Harrisburg, Pa., April 24–25, 1959.

Philadelphia Roentgen Ray Society
Secretary, Dr. Roderick L. Tondreau, 3400 Spruce St., Philadelphia 4, Pa. Meets first Thursday of each month, at 5 P.M., from October to May in Thompson Hall, College of Physicians.

Pittsburgh Roentgen Society
Secretary, Dr. Edwin Beck, 3500 Fifth Ave., Pittsburgh 13, Pa. Meets second Wednesday of month, October through June at Park Schenley Restaurant.

Radiological Section, Baltimore Medical Society
Secretary, Dr. James K. V. Willson, 1100 N. Charles St., Baltimore 1, Md. Meets third Tuesday each month, September to May, inclusive.

Radiological Section, Southern Medical Association
Secretary, Dr. Ted F. Leigh, Emory University, Georgia.

Radiological Society of Greater Cincinnati
Secretary, Dr. Warner Peck, Carew Tower St., Cincinnati 2, Ohio. Meets monthly from September to May on first Monday of each month at 7:30 P.M. at the Cincinnati General Hospital.

Radiological Society of Hawaii
Secretary, Dr. Robert G. Rigler, Straub Clinic, 1020 Kapiolani St., Honolulu 14, Hawaii. Meets third Monday of each month alternately at 4:30 P.M. and 7:30 P.M.

Radiological Society of Greater Kansas City
Secretary, Dr. Samuel B. Chapman, Jr., 830 Argyle Bldg., Kansas City, Mo. Meets last Friday of each month.

Radiological Society of Kansas City
Secretary, Dr. Arthur B. Smith, 800 Argyle Bldg., Kansas City, Mo. Meets third Thursday of each month.

Radiological Society of Louisiana
Secretary, Dr. Seymour Ochsner, Ochsner Clinic, New Orleans 15, La. Meets annually during Louisiana State Medical Society meeting.

Radiological Society of New Jersey
Secretary, Dr. Andrew P. Dedick, Jr., 67 E. Front St., Red Bank, N. J. Meets at Atlantic City at time of State Medical Society and in November in Newark, N. J.

Radiological Society of New York State
Secretary-Treasurer, Dr Mario C. Gian, 610 Niagara St., Buffalo 1, N. Y. Annual meeting: To be announced.

Radiological Society of South Dakota
Secretary-Treasurer, Dr. Donald J. Peik, 303 S. Minnesota Ave., Sioux Falls, S. D.

Radiological Society of Southern California
Secretary, Dr. Harold P. Tompkins, 658 S. Westlake, Los Angeles 57, Calif.

Redwood Empire Radiological Society
Secretary, Dr. Lee E. Titus, 164 W. Napa St., Sonoma, Calif. Meets second Monday every other month.

Richmond County Radiological Society
Secretary, Dr. W. F. Hamilton, Jr., University Hospital, Augusta, Ga. Meets first Thursday of each month at various hospitals.

Rochester Roentgen Ray Society, Rochester, N. Y.
Secretary, Dr. John W. Colgan, 277 Alexander St., Rochester 18, N. Y. Meets at 8:15 P.M. on the last Monday of each month, September through May, at Strong Memorial Hospital.

Rocky Mountain Radiological Society
Secretary, Dr. John H. Freed, 4200 East Ninth Ave., Denver 20, Colo. Annual meeting: Shirley-Savoy Hotel, Denver, Colorado, Aug. 20–22, 1959.

San Antonio-Military Radiological Society
Secretary, Dr. Hugo F. Elmendorf, Jr., 730 Medical Arts Bldg., San Antonio 5, Texas. Meets third Wednesday each month in Fort Sam Houston Officer's Club at 6:30 P.M.

San Diego Radiological Society
Secretary, Dr. Stanley A. Moore, 2466 First Ave., San Diego 1, Calif. Meets first Wednesday of each month at the University Club.

San Francisco Radiological Society
Secretary, Dr. Irma Smith, 450 Sutter St., San Francisco 8, Calif. Meets quarterly at Grison's Steak House.

Section on Radiology, California Medical Association
Secretary, Dr. William H. Graham, 630 East Santa Clara St., San Jose, Calif.

Section on Radiology, Connecticut State Medical Society
Secretary, Dr. Ralph J. Littwin, Bristol Hospital, Bristol, Conn. Meetings are held bi-monthly.

Section on Radiology, Medical Society of the District of Columbia
Secretary, Dr. Charles E. Bickham, Jr., 1835 Eye St., N.W., Washington 6, D. C. Meets Medical Society Library, third Wednesday of January, March, May and October at 8:00 P.M.

Section on Radiology, Illinois State Medical Society
Secretary, Dr. William Meszaros, 1825 W. Harrison St., Chicago, Ill.

Shreveport Radiological Club
Secretary, W. R. Harwell, 608 Travis St., Shreveport, La. Meets monthly on third Wednesday, at 7:30 P.M. September to May inclusive.

Society of Nuclear Medicine
Secretary, Dr. Robert W. Lackey, 452 Metropolitan Bldg., Denver 2, Colo. Annual meeting: To be announced.

South Bay Radiological Society
Secretary, Dr. Stanford B. Rossiter, 1111 University Dr., Menlo Park, Calif. Meets second Wednesday of each month.

South Carolina Radiological Society
Secretary, Dr. Wayne Reeser, 804 Burroughs St., Conway, S. C. One meeting with South Carolina Medical Association in May, others arranged by President.

Southern Radiological Conference
Secretary, Dr. Marshall Eskridge, Mobile Infirmary, Mobile, Ala.

Southwestern Radiological Society
Secretary, Dr. Gordon Black, Suite 2-A, El Paso Medical Center, 1501 Arizona, El Paso, Texas. Meets second Tuesday of each month.

Tennessee Radiological Society
Secretary, Dr. James J. Range, P.O. Box 324, Johnson City, Tenn. Meets annually at the time and place of the Tennessee State Medical Association.

Texas Radiological Society
Secretary, Dr. J. E. Miller, 3500 Gaston Ave., Dallas 10, Texas. Next meeting January 30 and 31, 1959, Statler-Hilton Hotel, Dallas, Texas.

Tri-State Radiological Society
Secretary, Dr. James R. Mathews, 118 S. E. First St., Evansville, Ind. Meets last Wednesday of Oct., Jan., March and May, 8:00 P.M. at Elks' Club in Evansville.

University of Michigan Department of Roentgenology Staff Meeting
Meets each Monday evening from September to June, at 7:00 P.M. at University Hospital.

University of Wisconsin Radiological Conference
Secretary, Dr. E. A. Pohle, 1300 University Ave., Madison, Wis. Meets first and third Thursdays 4:00 to 5:00 P.M., September to May, Service Memorial Institute.

Upper Peninsula Radiological Society
Secretary, Dr. A. Gonty, Menominee, Mich. Meets quarterly.

Utah State Radiological Society
Secretary, Dr. Angus K. Wilson, 343 S. Main St., Salt Lake City 1, Utah. Meets fourth Wednesday in January, March, May, September and November at Holy Cross Hospital.

VIRGINIA RADIOLOGICAL SOCIETY
Secretary, Dr. Frank A. Kearney, II, 110 S. Curry St., Phoebus, Va. Meets annually in October.

WASHINGTON STATE RADIOLOGICAL SOCIETY
Secretary, Dr. Wayne A. Chesledon, 306 Stimson Bldg., Seattle 1, Wash. Meets fourth Monday of each month from September through May at 610 Pine St., Seattle.

WEST VIRGINIA RADIOLOGICAL SOCIETY
Secretary, Dr. Karl J. Myers, 112 N. Woods St., Philippi, W. Va. Meets concurrently with annual meeting of West Virginia State Medical Society; other meetings arranged by program committee.

WESTCHESTER RADIOLOGICAL SOCIETY
Secretary, Dr. Arnold Myron Wald, 406 Boston Post Road, Port Chester, N. Y. Meets on third Tuesday of January and October and on two other dates.

WISCONSIN RADIOLOGICAL SOCIETY
Secretary, Dr. Farrell F. Golden, 5221 Tonyawatha Trail, Madison 4, Wis. Special meetings held during year; annual meeting each spring at Madison, Wis.

X-RAY STUDY CLUB OF SAN FRANCISCO
Secretary, Dr. John H. Heald, 450 Sutter St., San Francisco 8, Calif. Meets monthly, third Thursday at 7:30 P.M., Children's Hospital, September through June.

CUBA, MEXICO, PUERTO RICO AND CENTRAL AMERICA

ASOCIACIÓN DE RADIÓLOGOS DE CENTRO AMERICA Y PANAMÁ
Comprising: Guatemala, El Salvador, Honduras, Nicaragua, Costa Rica and Panamá, *Secretary-General*, Dr. Roberto Calderón, Calle Central Deste No. 218, Managua, Nicaragua. Meets annually in a rotating manner in the six countries.

SOCIEDAD DE RADIOLOGÍA DE EL SALVADOR
Secretary, Dr. Rafael Vega Gómez.

SOCIEDAD DE RADIOLOGÍA DE GUATEMALA
Secretary, Dr. Carlos E. Escobar, 9ª. Calle A 0-05, Zona 1, Guatemala.

SOCIEDAD DE RADIOLOGÍA Y FISIOTERAPÍA CUBANA
Secretary, Dr. Miguel A. García Plasencia, Hospital Curie, 29 y F, Vedado, Habana, Cuba. Meets monthly at Curie Hospital.

SOCIEDAD COSTARRICENSE DE RADIOLOGIA
Secretary, Dr. James Fernández Carballo, Apartado VIII, San José, Costa Rica.

SOCIEDAD MEXICANA DE RADIOLOGÍA, A. C.
Calle del Oro No. 15, México 7, D. F.
Secretary-General, Dr. Guillermo Santín. Meets first Monday of each month.

ASOCIACIÓN PUERTORRIQUEÑA DE RADIOLOGÍA
Secretary, Dr. R. B. Díaz Bonnet, Suite 504, Professional Bldg., Santurce, Puerto Rico.

SOCIEDAD RADIOLÓGICA PANAMEÑA
Secretary, Dr. L. Arrieta Sánchez, Apartado No. 86, Panamá, R. de P. Meets monthly in a department of radiology of a local hospital, chosen at preceding meeting.

BRITISH EMPIRE

ASSOCIATION OF RADIOLOGISTS OF THE PROVINCE OF QUEBEC
Secretary, Dr. Isadore Sedlezky, 3755 Cote St. Catherine Rd., Montreal, Que. Meets four times a year.

BRITISH INSTITUTE OF RADIOLOGY INCORPORATED WITH THE RÖNTGEN SOCIETY
Honorary Secretary, Dr. John Blewett, 32 Welbeck St., London, W. 1. Meets monthly from October until May.

FACULTY OF RADIOLOGISTS
Honorary Secretary, Dr. R. A. Kemp Harper, 47 Lincoln's Inn Fields, London, W.C.2, England.

SECTION OF RADIOLOGY OF THE ROYAL SOCIETY OF MEDICINE (CONFINED TO MEDICAL MEMBERS)
Meets third Friday each month at 4:45 P.M. at the Royal Society of Medicine, 1 Wimpole St., London, W. 1.

CANADIAN ASSOCIATION OF RADIOLOGISTS
Honorary Secretary, Dr. Guillaume Gill, *Associate Honorary Secretary*, Dr. Robert G. Fraser, 1555 Summerhill Ave., Montreal 25, Que. Meetings January and June.

SECTION OF RADIOLOGY, CANADIAN MEDICAL ASSOCIATION
Secretary, Dr. C. M. Jones, Inglis St., Ext. Halifax, N. S.

SOCIÉTÉ CANADIENNE-FRANÇAISE D'ELECTRO-RADIOLOGIE MÉDICALE
General Secretary, Dr. Louis Ivan Vallée, 1058 rue St-Denis, Montreal 18, Canada. Meets third Saturday each month.

TORONTO RADIOLOGICAL SOCIETY
Secretary, Dr. L. R. Harnick, Toronto Western Hospital, 399 Bathurst St., Toronto, Ontario. Meets second Monday of each month September through May.

COLLEGE OF RADIOLOGISTS OF AUSTRALASIA
Honorary Secretary, Dr. E. A. Booth, c/o British Medical Agency, 135 Macquarie St., Sydney, N.S.W., Australia.

SOUTH AMERICA

ASOCIACIÓN ARGENTINA DE RADIOLOGÍA
Secretary, Dr. Lidio G. Mosca, Avda. Gral. Paz 151, Córdoba, Argentina. Meetings held monthly.

O COLÉGIO BRASILEIRO DE RADIOLOGIA
Secretary-General, Dr. Walter Bomfins Pontes. Seat: Rua Major Quedinho, 99-2°. Andar, São Paulo, Brazil.

SOCIEDAD ARGENTINA DE RADIOLOGÍA, JUNTA CENTRAL, BUENOS AIRES
Secretary, Dr. Juan L. O. Ambrogna, Montevideo 745, Buenos Aires. Meetings are held monthly.

SOCIEDAD BOLIVANA DE RADIOLOGÍA
Secretary, Dr. Javier Prada Méndez, Casilla 1596, La Paz, Bolivia. Meets monthly. General assembly once every two years.

SOCIEDADE BRASILEIRA DE RADIOLOGIA MEDICA
Secretary, Dr. Nicola Caminha, Av. Mem. de Sa, Rio de Janeiro, Brazil. Meets monthly, except during January, February and March.

SOCIEDADE BRASILEIRA DE RADIOTERAPIA
Secretary, Dr. Oscar Rocha von Pfuhl, Av. Brigadeiro Luiz Antonio, 644 São Paulo, Brazil. Meets monthly on second Wednesday at 9:00 P.M. in São Paulo at Av. Brigadeiro Luiz Antonio, 644.

SOCIEDAD CHILENA DE RADIOLOGÍA
Secretary, Dr. Juan Sabbagh Dacla, Merced 565, Santiago, Chile. Meets fourth Friday of each month.

SOCIEDAD COLOMBIANA DE RADIOLOGIA
Secretary, Dr. Alberto Mejia Dzg., Carrera 13, No. 25-31, Apartado aéreo No. 5804, Bogotá, Colombia. Meets last Thursday of each month.

SOCIEDAD ECUATORIANA DE RADIOLOGÍA Y FISIOTERAPÍA
Secretary, Dr. Publio Vargas P. Casilla 1242 Guayaquil, Ecuador.

SOCIEDAD PARAGUAYA DE RADIOLOGÍA
Secretary, Dr. Miguel González Addone, 15 de Agosto 322, Asunción, Paraguay.

SOCIEDAD PERUANA DE RADIOLOGIA
Secretary, Dr. Luis Pinillos Ganoza, Apartado 2306, Lima, Perú. Meets monthly except during January, February and March, at Asociación Médica Peruana "Daniel A. Carrión," Villalta 218, Lima.

SOCIEDAD DE RADIOLOGIA DEL ATLANTICO
Secretary, Dr. Raul Fernandez, Calle 40 #41-110, Baranquilla, Colombia. Society meets monthly at the Instituto de Radiologia.

SOCIEDAD DE RADIOLOGÍA, CANCEROLOGÍA Y FÍSICA MÉDICA DEL URUGUAY
Secretary-General, Dr. Ricardo Parada, Av. Agraciada 1464, piso B, Montevideo, Uruguay.

SOCIEDADE DE RADIOLOGIA DE PERNAMBUCO
Secretary, Dr. Manoel Medeiros, Instituto de Radiologia da Faculdade de Medicina da Universidade do Recife, Caixa Postal 505, Pernambuco, Brazil.

SOCIEDAD VENEZOLANA DE RADIOLOGÍA
Secretary-General, Dr. Sebastian Núñez Mier y Terán,

Apartado No. 9362, Caracas, Venezuela. Meets monthly third Friday at Colegio Médico del Distrito Federal, Caracas.

Continental Europe

Österreichische Röntgen-Gesellschaft
President, Dr. Konrad Weiss, Mariannengasse 10, Vienna 9, Austria. Meets second Tuesday of each month in Allgemeine Poliklinik.

Société Belge de Radiologie
General Secretary, Dr. S. Masy, 256 Chaussée de Wavre, Heverlee-lez-Louvain, Belgium. Meets in February, March, May, June, October, November and December.

Société Française d'Electroradiologie Médicale, and its branches: Société du Sud-Ouest, du Littoral Méditerranéen, du Centre et du Lyonnais, du Nord, de l'Ouest, de l'Est, et d'Alger et d'Afrique du Nord. Central Society meets third Monday of each month, except during July, August and September, rue de Seine 12, Paris.
Secretary-General, Dr. Ch. Proux, 9, rue Daru, Paris 8e, France.

Ceskoslovensk společnost pro Rëntgenologii a Radiologii v Praze
Secretary, Dr. Roman Bláha, Praha xii, stát. nemocnice, Czechoslovakia. Meets monthly except during July, August, and September. Annual general meeting.

Deutsche Röntgengesellschaft
Secretary, Professor Dr. med. H. Lossen, Universitäts-Röntgeninstitut. Lagenbeckstr. 1, Mainz, Germany. Annual meeting: To be announced.

Società Italiana di Radiologia Medica e di Medicina Nucleare
Secretary, Dr. Ettore Conte, Ospedale Mauriziano, Torino, Italy. Meets annually.

Nederlandse Vereniging voor Electrologie en Röntgenologie
Secretary, Dr. J. R. von Ronnen, Violenweg 14, den Haag, Netherlands.

Scandinavian Roentgen Societies
The Scandinavian roentgen societies have formed a joint association called the Northern Association for Medical Radiology, meeting every second year in the different countries belonging to the Association.

Sociedad Española de Radiologia y Electrologia
Secretary, Dr. D. Aureo Gutierrez Churruca, Esparteros, No. 9, Madrid, Spain. Meets monthly in Madrid.

Schweizerische Röntgengesellschaft (Société Suisse de Radiologie)
Secretary, Dr. Max Hopf, Effingerstrasse 47, Bern, Switzerland.

India

Indian Radiological Association
Secretary, Dr. R. F. Sethna, Navsari Building, Hornby Road, Bombay 1, India.

The next list of Meetings of Radiological Societies will be published in the March issue of the Journal.

INTER-AMERICAN COLLEGE OF RADIOLOGY

The Sixth Inter-American Congress of Radiology was held in Lima, Perú on November 2 to 8, 1958. The program was excellent and very well organized and the social activities, as usual, were most enjoyable.

On this occasion, a special Convocation of the American College of Radiology was held. The following were awarded Honorary Fellowships:

Doctor Agustin Castellanos of Cuba
Doctor Narno Dorbecker of México
Doctor Pedro Gonzáles Rincones of Venezuela
Doctor Mathias Roxo-Nobre of Brazil
Doctor Vicente Ubillús of Perú

Doctor Oscar Soto of Perú, President of the Congress, was awarded a special Diploma of Honor at this ceremony.

Brazil was honored in being selected the Country for arranging the Seventh Inter-American Congress of Radiology in 1961. Doctor J. Manuel Viamonte, Sr. of Havana was elected President. Doctor Laura Fariñas of Havana was elected Secretary and Doctor Eduardo Rivero of Havana was elected Treasurer.

NINTH INTERNATIONAL CONGRESS OF RADIOLOGY

As has previously been announced, an industrial exhibition will be held on the occasion of the Ninth International Congress of Radiology from July 23 to 30, 1959 in Munich. On an exhibition area of over 8,000 square meters, more than 80 exhibitors from 14 countries will show a comprehensive cross-section of the current state of radiologic technology and related fields in medicine.

Information concerning this exhibition can be obtained on application to the Committee for the Industrial Exhibition, Mönckebergstr. 7, Hamburg 1, Germany.

FOURTH INTERNATIONAL COURSE ON TOMOGRAPHY

The Fourth International Course on Tomography will be held at the Institute of Radiology, University of Genova, under the direction of Prof. Alessandro Vallebona, in September–October, 1959.

The course will last eight days and deal particularly with the recent progress in tomographic methods. All lectures, while read in the original language, will be contemporarily translated into Italian, French, English, German and Spanish.

Those who are interested in the course are asked to contact Prof. Neopolo Macarini, General Secretary, Istituto di Radiologia della Università, Ospedale San Martino, Genova, Italy, for whatever details they desire.

THE ROCKY MOUNTAIN RADIOLOGICAL SOCIETY

At the last Annual Meeting of the Rocky Mountain Radiological Society, the following officers for 1959 were elected: President, Dr. George A. Unfug; President-Elect, Dr. Gerald S. Maresh; 1st Vice-President, Dr. Peter E. Russo; 2nd Vice-President, Dr. Paul E. Re Pass; Secretary-Treasurer, Dr. John H. Freed; and Historian, Dr. H. Milton Berg.

The next annual meeting will be held on August 20 to 22, 1959 at the Shirley-Savoy Hotel in Denver, Colorado.

EAST TENNESSEE RADIOLOGICAL SOCIETY

A group of representative radiologists met in Gatlinburg, Tennessee, on September 6, 1958, and formed the East Tennessee Radiological Society. The following officers were elected: President, Dr. Edward K. Carter of Kingsport; President-Elect, Dr. Eugene Abercrombie of Knoxville; Vice President, Dr. John Higgason of Chattanooga; and Secretary-Treasurer, Dr. Charles W. Reavis of Chattanooga.

The organization will meet in January and September.

RADIOLOGICAL COURSE TO BE GIVEN AT UNIVERSITY OF KANSAS MEDICAL CENTER

A course on radiology will be given at the University of Kansas Medical Center from

February 9 to 11, 1959. The speakers will cover diagnostic roentgenological subjects, isotopes, and radiation therapy.

The list of the speakers includes: Jack Ball, Ph.D., Picker X-ray Company; E. F. Van Epps, M.D., Iowa University Medical School; Melvin Figley, M.D., University of Washington Medical School; Colon Holman, M.D., Mayo Clinic, Rochester, Minnesota; Charles Martin, M.D., Dallas, Texas; Edith Quimby, Sc.D., New York, New York; John Reeves, M.D., University of Florida Medical School; and Don Weir, M.D., St. Louis, Missouri.

For further information relative to the course, address G. M. Tice, M.D., Radiologist, University of Kansas Medical Center, Kansas City, Kansas.

THE AMERICAN SOCIETY OF X-RAY TECHNICIANS

The American Society of X-ray Technicians is holding its thirty-first annual convention at the Shirley-Savoy Hotel in Denver, Colorado, July 4 through July 9, 1959. The Publicity Chairman is Barbara Riley Hunt, R. T., 1686 S. Bryant, Denver 9, Colorado.

We regret to announce the sudden death on November 19, 1958, in Chicago of Dr. Warren W. Furey, distinguished member of the American Roentgen Ray Society and member of the Board of Trustees of the American Medical Association.

THE AMERICAN RADIUM SOCIETY

TENTATIVE PROGRAM

The following is the tentative program arranged by the Program Committee and the Committee on Arrangements under the Chairmanships of President Milford D. Schulz and Doctor Charles C. Stetson, respectively, for the Forty-first Annual Meeting of the American Radium Society to be held at The Homestead, Hot Springs, Virginia, Sunday through Wednesday, April 5, 6, 7 and 8, 1959.

Sunday April 5, 1959

2:00–5:00 P.M.
Registration

Monday, April 6, 1959

8:30 A.M.
First Executive Session

9:00 A.M. Onward.
Registration

9:00 A.M.
Opening of the Forty-first Annual Meeting and Presidential Address

9:30 A.M.
First Scientific Session
Theodore R. Miller, M.D., Chairman

Colloquium: Problems in the Management of Cancer of the Larynx. Ralph M. Caulk, M.D., Washington, D. C., Moderator, Simeon T. Cantril, M.D., Seattle, Robert Robbins, M.D., Philadelphia, Calvin T. Klopp, M.D., Washington, D. C., and LeRoy A. Schall, M.D. (by invitation), Boston.

Recess

Cancer of the Nasopharynx. Robert Robbins, M.D., Philadelphia, and John V. Blady, M.D., Philadelphia.

The Place of Radiotherapy in the Treatment of Tumors of the Temporal Bone. Vera M. Dalley, D.M.R.T. (by invitation), London.

Combined Techniques, External Radiation and Interstitial Radium in the Treatment of Head and Neck Tumors. Carlos A. Cuccia, M.D. (by invitation), Baltimore.

Discussions of Morning Presentations

1:00 P.M.
Adjournment

2:30–4:00 P.M.
Informal Discussion Groups, Presentation of Unscheduled and Impromptu Papers, Scientific Cinema, etc.

5:30 P.M.
The Janeway Lecture.
James T. Case, M.D.

6:30 P.M.
Social Hour

7:30 P.M.
Informal Dinner

9:00 P.M.
Dancing ad libitum

Tuesday, April 7, 1959

8:30 A.M.
Second Executive Session

9:00 A.M.
Registration

9:00 A.M.
Second Scientific Session
James F. Nolan, M.D., Chairman

Colloquium: Causes of Failure in the Treatment of Cancer of the Oral Cavity. William S. MacComb, M.D., Houston, Moderator, Simeon T. Cantril, M.D., Seattle, Gilbert H. Fletcher, M.D., Houston, Lewis W. Guiss, M.D., Los Angeles, and Arthur G. James, M.D., Columbus.

Recess

Roentgen Therapy of Skin and Lip Cancer: Factors Influencing Success and Failure. Carl von Essen, M.D. (by invitation), San Francisco.

Problems in Planning Radiation for Post-operative and/or Post-radiation Recurrences in Gynecologic Cancer. Rieva Rosh, M.D., New York.

Seminoma: The Treatment of Late Recurrence, Metastases and Second Primary Tumor. Milton Friedman, M.D., New York.

Radiation Nephritis. Bryan L. Redd, Jr., M.D. (by invitation), Atlanta.

Radiation Myelitis. John B. Dynes, M.D. (by invitation), Boston, and Magnus I. Smedal, M.D., Boston.

Discussions of Morning Presentations

1:00 P.M.
Adjournment

2:30–4:00 P.M.
Informal Discussion Groups, Presentation of Unscheduled and Impromptu Papers, Scientific Cinema, etc.

6:30 P.M.
Reception for Members and Guests

7:30 P.M.
Banquet and Presentation of Janeway Medal

9:00 P.M.
Entertainment

Wednesday, April 8, 1959

8:30 A.M.
Third Executive Session

9:00 A.M.
Third Scientific Session
Theodore P. Eberhard, M.D., Chairman

Survival of More Than Ten Years in Hodgkin's Disease. K. L. Krabbenhoft, M.D., Detroit, J. C. Cook, M.D., Detroit, and T. Leucutia, M.D., Detroit.

Marrow Transplantation after Exposure to Lethal Radiation. Joseph W. Ferrebee, M.D. (by invitation), Cooperstown, New York.

The Psychiatrist and the Cancer Patient. Howard H. Ashbury, M.D., Staunton, Va.

Common Medical Problems in Patients Undergoing Radiation Therapy. Arvin Glicksman, M.D. (by invitation), New York, and James J. Nickson, M.D., New York.

The Treatment of Retinoblastoma by X-Ray Alone, and by the Combination of X-Ray and TEM. Norah duV. Tapley, M.D. (by invitation), New York.

Recess

Difficulties in Prognosis of Neuroblastoma: Review of 150 Cases. Harold Dargeon, M.D., New York

The Moving Strip Technique in Treatment of Cancer of the Breast. F. Batley, M.B., D.M.R.T., Kingston, Ontario.

Ir^{192} Implantation in the Internal Mammary Vessels for Breast Cancer. Richard D. Brasfield, M.D. (by invitation), New York, and Ulrich K. Henschke, M.D., NewYork.

Unusual Radium Implants in the Treatment of Cancer. Fernando G. Bloedorn, M.D., Baltimore.

Radioactive Gold in the Treatment of Papillomatosis of the Bladder. Robert J. Dickson, M.D. (by invitation), Baltimore.

Discussions of Morning Papers

Closing Ceremonies and Introduction of New Officers

1:00 P.M. Adjournment

BOOK REVIEWS

Books sent for review are acknowledged under: Books Received. This must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interest of our readers as space permits.

ACTION OF RADIATION ON TISSUES; AN INTRODUCTION TO RADIOTHERAPY. A. Lacassagne, Chief of Service of Pasteur Institute, Director of the Radium Institute (Biological and Therapeutic Sections); and G. Gricouroff, Chief of the Laboratory of the Curie Foundation (Radium Institute); translated by Clarence C. Lushbaugh, M.D., and Gretchen R. Riese, M.S., Los Alamos Scientific Laboratory, University of California. Second edition. Cloth. Price, $6.25. Pp. 199, with 17 illustrations. Grune & Stratton, Inc., 381 Fourth Avenue, New York 16, New York, 1958.

In 1957 the reviewer proposed to the authors that, as a labor of love, he be permitted to translate the French edition of this work into English and learned that it was already under way by Clarence C. Lushbaugh, M.D. and Gretchen R. Riese, M.S. of Los Alamos Scientific Laboratory. He was pleased to learn that the volume would be made available to those who are unable to study the original classics which form the basis of this succinct account of radiobiology. This small monograph is basic information for all those interested in clinical radiotherapy and the newer edition contains a remarkable synthesis of more recent radiobiologic data gleaned from the impetus given to radiobiology following the release of nuclear energy. In addition to the bibliography prepared by the authors, the translators have added bibliographic references gleaned from their own readings and experience. Dr. Antoine Lacassagne needs no introduction to radiotherapists and radiobiologists. Dr. Georges Gricouroff has for many years been Chief of the Laboratories of Histopathology of the Curie Foundation, Paris, where he has been able to carefully study the histopathology of radiation effects, both clinical and experimental.

Although radiotherapy is primarily concerned with the ultimate effect of irradiation on malignant tissue, its limitations lie in normal tissue tolerance, which in itself is the restraining guide to major radiation injury and hence the capabilities of radiotherapy as a palliative and curative agent. The volume deals with the action of radiations on normal tissues and the early and late manifestations which are produced. In this sense it is a description of *radiophysiology*, and to a lesser extent radiopathology.

Not only is the monograph the best available in English to the student of radiotherapy but in it will be found a remarkably complete review of radiobiology written by those who have themselves contributed so much to the early development. The translators have performed an immeasurable service to American radiotherapy by their labors as all will appreciate who will spend some evenings reading and rereading this account.

SIMEON T. CANTRIL, M.D.

LA ROENTGENTHÉRAPIE DES AFFECTIONS RHUMATISMALES. By Pierre Pizon. Paper. Price, 2,800 fr. Pp. 276, with 60 illustrations. Masson et C^{ie}, Editeurs, 120 boulevard Saint-Germain, Paris 6^{e}, France, 1957.

This work is a two-fold study: a clinical analysis of rheumatalgia and a technical analysis of roentgen therapy applied to rheumatismal affections. The author's experience is based on more than 1,000 personal observations.

The first part is primarily of medical interest. All of the so-called rheumatic affections are reviewed one after another. The nature of every entity dealt with is first precisely defined, then the clinical synptoms are carefully evaluated, with special attention given to the pathogenesis. In most cases a correlation between the symptoms and the roentgenographic appearance is offered. To end every chapter, the author presents a review of the currently used treatments for the disease being discussed as against roentgen therapy.

The author calls attention to certain fundamental facts. For example, the pain attributed to a protruding intervertebral disk has never been conclusively explained; the pathogenesis of a cervicobrachialgia or a sciatica might be related to a viral origin or a concealed vascular disorder; also, the neurovegetative nature of rheumatic pain has never been physiologically demonstrated.

In every chapter of the book, a reader might reproach the author for the use of names in describing symptoms, syndromes, or clinical signs and tests. The nomenclature of rheumatic diseases differs from that of the North American continent to which we are accustomed. However the clinical descriptions permit us to identify the pathologic entities.

The second part deals with the technical aspects of roentgen therapy.

The author, utilizing a combination of factors, calculates what he calls the cumulative "weight-doses" which, according to him, should be sufficient for successful treatment of all rheumatalgias. He deems important the knowledge of the absorption coefficient in tissues, especially in bone, the bony volume irradiated, and the effect of variations in the physical factors encountered in tissue irradiation.

The author then discusses the conditions of a rational irradiation and puts forth a somewhat codified formula for the treatment of all rheumatic pains. Here again one is apt to reproach the author for his tendency to reduce to a "mathematical formula" the irradiation treatment of a pain. The book also includes a discussion on the hazards and dangers encountered with this irradiation. A final chapter on physics touches on the computation of the energy absorbed by bone and on the distribution of ionization in tissues.

The high percentage of cure and improvement attributed to roentgen therapy (75 per cent in coxarthria and 91 per cent in lumbago, sciatica and cervicobrachialgia) points out the value of irradiation as an effective treatment in controlling rheumatic conditions.

Robert L'Abbé, M.D.

A Text-Book of X-Ray Diagnosis by British Authors in Four Volumes. Volume III. Edited by S. Cochrane Shanks, *C.B.E.*, M.D., F.R.C.P., F.F.R., Director, X-Ray Diagnostic Department, University College Hospital, London; and Peter Kerley, *C.V.O.*, *C.B.E.*, M.D., F.R.C.P., F.F.R., D.M.R.E., Director, X-Ray Department, Westminster Hospital, Radiologist, National Heart Hospital, London. Third edition. Cloth. Pp. 883, with 802 illustrations. Price, $23. W. B. Saunders Company, 218 West Washington Square, Philadelphia, Pennsylvania, 1958.

The first volume of this third edition appeared late in 1957. The third volume has come out, but the second (as well as the fourth and last) must still be republished. When compared with the corresponding part of the second edition (1950), the third volume contains an additional 53 pages and 108 illustrations. The changes include mainly points of technique, such as new procedures and contrast media. Kerley has entirely rewritten Chapter XXXV on the examination of the biliary tract, while C. Rohan Williams advocates water-soluble media as a replacement for lipiodol in hysterosalpingography. A. S. Johnstone and P. G. Keates (who revised the section on the urinary tract, authored in the previous edition by Shanks and Johnstone) bring details on presacral gas insufflation and renal arteriography. Chapter XXXVI, which in the second edition starts with the assurance that there is no evidence that standard pelvimetry is harmful to either mother or fetus, begins in the third edition with the mention that Oxford University's Department of Social Medicine has published in 1956 a study which tends to incriminate roentgenographic pelvimetry performed during pregnancy as a cause for increased incidence of leukemia in the offspring. In chapter XIV (pelvimetric techniques), the subchapters from the second edition, written by Robert P. Ball (New York), Clark Nicholson, Paul C. Swenson (Philadelphia), and Herbert Thoms (New Haven, Connecticut) have been deleted; the subchapters by J. Chassar Moir (Oxford, England), by the late Howard C. Moloy (New York), and by C. Rohan Williams (London), the author of the entire chapter, are essentially unchanged. To these were added new subchapters by Peter Allen (New Plymouth, New Zealand), and by J. Blair Hartley (Manchester, England). A few recent titles have been included in the short bibliographies appended to the subdivisions.

It is felt that these changes are in keeping with the general outline of the work, and have succeeded in "modernizing" the text. Like the first volume of the third edition, this is a very dignified scion of the British classic of roentgenologic diagnosis, and as such it is highly recommended both as a textbook and as a reference manual.

E. R. N. Grigg, M.D.

Duodénum et Pancréas. By Guy Albot, Médecin de l'Hôtel-Dieu; and F. Poilleux, Chirurgien de l'Hôpital Corentin-Celton.

Paper. Price, 3,500 fr. Pp. 296, with 126 illustrations. Masson et C^ie, Editeurs, 120 boulevard Saint-Germain, Paris 6^e, France, 1957.

This book is the fifth of the series presented by Actualités hépato-gastro-entérologiques de l'Hôtel-Dieu, and is devoted to the study of two poorly understood organs, namely the duodenum and the pancreas.

The main subjects include: (1) tumoral lesions of the duodenum, megaduodenum, Vater ampullomas; (2) duodenal spasms and duodenobiliary interactions; (3) the duodenum after gastric operations; (4) modern exploratory methods of the pancreas; (5) lithiasis of the Wirsung's canal and pancreas; (6) chronic pancreatitis without biliary components; (7) pancreatic cysts; and (8) hypoglycemic syndromes.

The authors give a thorough and up-to-date review of the physiopathology, pathogenesis and treatment of the various conditions affecting the duodenum and the pancreas.

Of special interest is the masterful study by Albot, Poilleux and Kapandji of the three sphincteral zones of the duodenum. These have been investigated by radiomanometry, cholecystography, barium meal and duodenal intubation. Spasms by these sphincters must be recognized and detected before and after any gastric intervention. Their discovery might explain some complications heretofore attributed to other causes. Dysfunction of these sphincters might have an influence on the type of biliary digestive anastomoses, the type of operative drainage, etc.

The functional disturbances of the duodenum after gastroenterostomy, the circulus viciosus, the afferent loop syndrome and stomal dysfunction after gastroenterostomy are meticulously analyzed and evaluated.

The book is well illustrated with roentgenographic reproductions, photographs of gross specimens and photomicrographs. It is highly recommended to surgeons, internists and radiologists whose problems and interests concern these two organs.

H. P. LÉVESQUE, M.D.

THE ALIMENTARY TRACT OF THE RUMINANT. By David Benzie and A. T. Phillipson, M.A., Ph.D., M.R.C.V.S., F.R.S.E. The Rowett Research Institute, Bucksburn, Aberdeenshire, Cloth. Price, $5.50. Pp. 103, with 54 plates. Charles C Thomas, 301 East Lawrence Avenue, Springfield, Illinois, 1958.

Modern, powerful equipment has made it possible for the authors, of the Rowett Research Institute, Aberdeen, to compile this much-needed contribution to ruminant physiology. It is timely in view of the recent, concerted efforts to uncover facts in this field.

The monograph gives a concise, clear discussion of the anatomy and physiology of the ruminant alimentary tract; just enough to prepare one for reading the many roentgenograms which make up the bulk of the volume. Each plate has on it several roentgenograms, and each roentgenogram is accompanied by a thumbnail sketch to point out the areas of importance. A cineroentgenographic sequence demonstrates the movements of the four parts of the stomach. The authors include a generous bibliography for anyone interested.

Ease of reference and reading is the forte of this text. In an effort to keep the thumbnail sketches uncluttered, a code and master key arrangement were devised. There is a minimum of textual material accompanying each plate.

A variety of animals representing the ruminant type were used—six kids, twelve lambs, twelve sheep, and four calves. Barium sulfate, given with the normal diet, and silver markers were used as radiopaque media. The time span of the roentgenograms depicts the developmental and physiologic changes in the ruminant stomach. The earliest stage is of a kid five and one-half hours after birth; the oldest is of a four year old ewe.

The authors are to be congratulated for a worthwhile contribution to this subject.

JOHN H. GREVE, D.V.M.

WESEN UND BEDEUTUNG DER ENCHONDRALEN DYSOSTOSEN. By Priv.-Doz. Dr. H. Mau, Heidelberg. Paper. Price, DM 27.—. Pp. 219, with 83 illustrations. Georg Thieme, Herdweg 63, Stuttgart, Germany, 1958.

This monograph deals with the many forms of dysostoses and the disturbances in ossification of cartilage in the growing skeleton, which originate on a congenital-hereditary basis. Chondrodystrophy, achondroplasia, chondrodysplasia, osteochondrodystrophy, dyschondroplasia and many other synonyms of basically the same disorder are used in the literature for the more or less typical enchondral dysostosis. More localized and epiphyseal types of the same disturbance as familiar osteochondritis, Ribbing's disease, Blount's disease, Thiemann's

disease, etc., may well be other forms of enchondral dysostosis. Gargoylism and chondrodystrophia calcificans may also belong in this large group of disturbances of calcification of cartilage.

The literature describing the different manifestations of these diseases is considered rather in detail, mainly in order to bring the different types into one large group. The author himself has observed 75 cases. He differentiates between two main types—the metaphyseal and the epiphyseal. Mixed types are probably the most common ones. Much attention is paid to the minor and minimal abnormalities. The roentgenologic manifestations are considered in detail. As much as possible, the anatomic and pathologic basis of the disorder is brought out. The genetic and hereditary nature of the dysostoses is stressed. In the opinion of the author, dysostotic individuals are predisposed to aseptic necrosis and early arthrosis deformans, especially when they occur bilaterally, familially and early in life. The combination of dysostosis with other skeletal disorders appears possible in many other diseases, such as cleidocranial dysostosis, osteogenesis imperfecta, arachnodactyly, Hurler's disease, chondromatosis, etc.

In order to demonstrate enchondral dysostosis as the cause or partial cause, roentgen examination, including lateral views, of the dorsolumbar spine, pelvis and hips, and wrists for bone age is essential. A good history of anomalies in the family and clinical measurement for determination of lack of normal growth are necessary.

An indirect constitutional dysostotic disposition in many such diseases could be the unifying explanation for many different syndromes and skeletal diseases. It is possible that the enchondral dysostosis is the most common congenital disease of the skeleton when it is considered in this way.

The booklet is well written and well illustrated. It represents a fascinating and provocative study which makes reading well worthwhile for any radiologist or orthopedic surgeon who is interested in these diseases.

Hans W. Hefke, M.D.

Fractures and Other Injuries. Edited by Edwin F. Cave, M.D. Cloth. Price, $28.00. Pp. 863, with 611 illustrations. Year Book Publishers, Inc., 200 E. Illinois Street, Chicago, 11, Illinois, 1958.

The Fracture Service and Fracture Clinic of the Massachusetts General Hospital was organized in 1917 by Charles L. Scudder. A statistical review of end results was presented by Philip D. Wilson in 1938 when he edited "Experience in the Management of Fractures and Dislocations." The present volume does not give statistical data but very complete advice for the management of all types of traumatic injuries.

This Service and Clinic has for many years done a superb job in the field of postgraduate teaching. This volume comes as a modern climax to an already enviable record. Each chapter in the volume was written by one or more of 39 contributors who have earned distinction in their field of interest.

This volume presents complete and excellent coverage of the methods and techniques of dealing with fractures. A plan for the organization of a fracture service is included. Chapters are devoted to metabolic response to trauma; the influence of trauma upon patients so affected; traumatic shock; the proper utilization of the x-ray service; and advice as to anesthesia in this field.

The relationships of bone injuries to those of all components of the nervous system are covered, as well as those relating to injuries of the chest, abdomen, genitourinary tract and vascular system. The effects of both heat and cold are well presented. A timely chapter on the value of rehabilitation is included.

The editorial board has compressed in a lucid and well organized manner as much knowledge in as few pages as I have ever encountered. It is truly a remarkable achievement. The illustrations are many. The line drawings are unusually illustrative. The book is easy to read and is well indexed. It is a little bulky to handle.

The men who have collaborated to give us this finished product are to be complimented. It will, I believe, mark a milestone in postgraduate teaching during this generation in America. It deserves a place in every hospital library and in the possession of every surgeon whose work is in the field of trauma.

Frank P. Walsh, M.D.

Étude Radiologique de la Circulation Veineuse du Membre Supérieur (Sujet normal). By Ercole Lavizzari and Valerio Ottolini. Paper. Price, 2,400 fr. Pp. 122, with 38 illustrations. Masson et Cie, Editeurs, 120

boulevard Saint-Germain, Paris 6e, France, 1958.

This monograph is a unique and interesting roentgenologic study of the venous circulation in the normal upper limb. The work is based on 228 phlebograms obtained in patients who were referred for intravenous pyelography but were otherwise considered normal from the angiologic viewpoint. The interrelations between morphologic and functional aspects of the venous systems were explored in great detail.

The investigation had three principal objectives: (1) the phlebographic appearance was studied under the following conditions: (a) injection of the contrast material into different veins, (b) variation of the level at which the injections were made, (c) use of different speeds of injection, and (d) modification of the hemodynamic factors in the limb (normal return, partial blocking, and circulation immediately after unblocking); (2) the authors studied the physiologic pathways of venous return in the normal upper limb at rest; and (3) they established the technical conditions to be followed to obtain characteristic phlebograms.

The book is illustrated with pertinent phlebographic reproductions and schematic drawings. It is recommended to vascular surgeons and radiologists and to all others interested in the venous anatomy of the upper extremity.

H. P. Lévesque, M.D.

BOOKS RECEIVED

Progress in Radiation Therapy. Edited by Franz Buschke, M.D., Professor of Radiology, University of California School of Medicine, San Francisco; with 13 contributors. Cloth. Price, $9.75. Pp. 284, with tables and figures. Grune & Stratton, Inc., 381 Fourth Avenue, New York 16, New York, 1958.

The Author Publisher Printer Complex. By Robert S. Gill. Third edition. Cloth. Price, $2.25. The Williams & Wilkins Company, Mount Royal and Guilford Avenues, Baltimore 2, Maryland, 1958.

The Ureterovesical Junction. By John A. Hutch, M.D., Clinical Instructor of Urology, University of California, San Francisco. Cloth. Price, $7.50. Pp. 178, with 96 illustrations. University of California Press, Berkeley 4, California, 1958.

Tumors and Tumorous Conditions of the Bones and Joints. By Henry L. Jaffe, M.D., Director of Laboratories and Pathologist, Hospital for Joint Diseases, New York, N. Y.; Consultant, Armed Forces Institute of Pathology, Washington, D. C. Cloth. Price, $18.50. Pp. 629, with 701 illustrations. Lea & Febiger, Washington Square, Philadelphia 6, Pennsylvania, 1958.

Radioactive Isotopes in Clinical Practice. By Edith H. Quimby, Sc.D., Professor of Radiology (Physics), College of Physicians and Surgeons, Columbia University, New York; Sergei Feitelberg, M.D., Director, Physics Department, The Mount Sinai Hospital, and Associate Clinical Professor of Radiology, College of Physicians and Surgeons, Columbia University, New York; and Solomon Silver, M.D., Attending Physician and Chief, Thyroid Clinic, The Mount Sinai Hospital, and Associate Clinical Professor of Medicine, College of Physicians and Surgeons, Columbia University, New York. Cloth. Price, $10.00. Pp. 451, with 97 illustrations. Lea & Febiger, Washington Square, Philadelphia 6, Pennsylvania, 1958.

Oral Roentgenographic Diagnosis. By Edward C. Stafne, Senior Consultant, Section of Dentistry and Oral Surgery, Mayo Clinic, and Professor of Dentistry and Oral Surgery, Mayo Foundation, Graduate School, University of Minnesota, Rochester, Minnesota. Cloth. Price, $14.50. Pp. 303, with 1,338 illustrations. W. B. Saunders Company, 218 West Washington Square, Philadelphia 5, Pennsylvania, 1958.

Hot Laboratory Equipment. Compiled by L. G. Stang, Jr. Second edition. Paper. Price, $2.50. Pp. 429, with 351 illustrations. Brookhaven National Laboratory operated for the United States Atomic Energy Commission. May be purchased from the Superintendent of Documents, U. S. Government Printing Office, Washington 25, D. C., 1958.

Berättelse från Styrelsen för Cancerföreningen I Stockholm över Verksamhetsåret 1957; Redogörelser för Verksamheten å Radiumhemmet, Radiopatologiska Institutionen Och Radiofysiska Institutionen Vid Konung Gustaf V:s Jubileumsklinik I Stockholm under År 1957. Index of Papers Published at the Radiumhemmet, the Institute of Radiopathology and the Institute of Radiophysics; Report of Dec. 31st, 1958, on Patients Registered at the Radiumhemmet 1921–1957. Paper. Pp. 154, with tables. L. K. Beckmans Boktryckeri, Stockholm, Sweden, 1958.

ABSTRACTS OF RADIOLOGICAL LITERATURE

Department Editor: T. Leucutia, M.D., Harper Hospital, Detroit 1, Michigan

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ROENTGEN DIAGNOSIS

Head

Sayers, Martin Peter, and Britt, Clarence I. Skull dehiscence and dural laceration in unrecognized familiar craniostenosis. *A.M.A. J. Dis. Child.*, May, 1958, *95*, 524–528. (Address: M. P. Sayers, 1275 Olentangy River Rd., Columbus 8, Ohio.)

The authors describe a case of craniostenosis of the scaphocephalic type in a three month old white girl who sustained a linear fracture of the right parietal bone. There was underlying dural laceration and right parietal soft tissue swelling which at surgery contained macerated brain fragments from the subgaleal fluid collection which overlay the 5 cm. dural laceration under the transverse fracture line. The dural tear was closed with a free graft of cranial periosteum and a 2 cm. midline strip of bone was removed to include the sagittal suture for therapy of the craniostenosis. Recurrence of the bulge at the operative site was noted 3 months later and at surgery a 3 cm. rupture was found at the site of the periosteal graft. Further repair of the laceration was performed with layers of pericranium sutured over the defect and this appeared to be of a sufficient strength to prevent recurrence.

The roentgenogram at the second admission demonstrated considerable widening of the defect created by linear craniectomy (synostectomy). The authors believe that the rapid brain expansion following synostectomy for craniostenosis jeopardizes any site for dural repair of lacerations.

Evidence is presented to substantiate the thesis that skull expansion is largely secondary to pressure from normal brain growth. Arrested or retarded skull growth and unusual head shape indicate the need for early roentgenographic examination to confirm the clinician's suspicion of craniostenosis.—*James F. Martin, M.D.*

Sutton, David. Radiology of cerebral angiomas. *J. Fac. Radiologists*, April, 1958, *10*, 90–96. (From: Maida Vale Hospital for Nervous Diseases, London, W. 9, England.)

Angiomatous malformations as recently as 1928 were considered rare by such writers as Cushing and Bailey, and Dandy, but since the advent of cerebral arteriography they have been found to be very common neurologic lesions. Plain roentgenograms may show abnormal vascular channels in the skull vault, and in particular hypertrophied and tortuous meningeal vascular channels—often associated with gross enlargement of the foramen spinosum. Calcification has also been described in angiomata on plain film examination in 10 to 24 per cent of cases. The typical findings consist of speckled calcification or several scattered flecks of calcium in the area of the tumor, resembling the calcified plaques seen in the walls of atheromatous vessels. Along with these calcified flecks one may sometimes see ring shadows of the type associated with aneurysms.

The angiographic investigations required depend upon the site and the size of the lesion. To demonstrate the entire anatomic extent of the lesion bilateral rather than simple unilateral carotid arteriography may be necessary. In other cases vertebral arteriography, sometimes with unilateral or bilateral carotid arteriography, may be required for satisfactory demonstration of the lesion.

The typical arteriovenous malformation is in effect a direct arteriovenous shunt. In a large angioma situated in one cerebral hemisphere angiography of the ipsilateral carotid artery may demonstrate hypertrophied arteries leading to the angioma. These hypertrophied arteries are fed by a hypertrophied main vessel, such as the middle cerebral artery, and this in turn is fed by a hypertrophied internal carotid artery on the affected side. Early opacification at arteriography is an important feature of the venous drainage of hemangiomas.

Air studies are indicated rarely in suspected cases of angiomatous malformation. In differential diagnosis lesions which may resemble angiomatous malformation include vascular malignant glioma, hemangioblastoma and an excessively vascular secondary deposit, this being illustrated in the paper by a case of secondary hypernephroma.

Some of the cases of angiomatous malformation are of particular interest to the ophthalmologist. Ophthalmologic findings which have been noted in these angiomatous lesions include periodic migrainous headaches with a visual aura, homonymous field defects, papilledema, pulsating exophthalmos, and defects of ocular movement of central type.—*Samuel G. Henderson, M.D.*

Danaraj, T. J. Haematogenous brain abscess complicating Fallot's tetralogy. *Proc. Alum. Ass. Malaya*, June, 1958, *11*, 80–87. (From: The Department of Medicine, University of Malaya, Singapore.)

The author notes that brain abscess, as a complication of congenital heart disease with a venous-arterial shunt, is not uncommon. Reference is made to Newton's paper in 1956 in which he reviewed 72 previously reported cases collected from the literature with 7 of his own. A cardiac malformation resulting in a central venous-arterial shunt was present in 67 (84.8 per cent) of the 79 cases and may have existed in the remainder. The commonest malformation was Fallot's tetralogy.

Four additional cases of brain abscess complicating Fallot's tetralogy are reported by the author. Complete case reports are given, including reproductions of roentgenograms and photographs of gross specimens. The importance of diagnosis is stressed

in view of the possibility of satisfactory treatment with antibiotics combined with surgical drainage.

Of the 7 cases reported by Newton, recovery occurred in 3 after antibiotic therapy and aspiration of the abscess. Of the 4 cases reported by the author, recovery was reported in two. Another was considered as recovered, but died suddenly eight months later. The fourth patient died before surgical intervention.—*D. S. Kellogg, M.D.*

NECK AND CHEST

SCHIEPPATI, EDUARDO. Mediastinal lymph node puncture through the tracheal carina. *Surg., Gynec. & Obst.*, Aug., 1958, *107*, 243–246. (From: The Thoracic Surgery Institute, Buenos Aires, Argentina.)

The author discusses a method which he described in 1949 for the endoscopic puncture of the tracheobronchial mediastinal lymph nodes through the tracheal carina.

When the mediastinal lymph nodes around the carina are involved and enlarged, the tracheobronchial carina as seen through the endoscope appears to be enlarged, deformed, rotated and less mobile. These conditions can also be observed in chronic inflammatory disease with traction on the carina and in other causes of compression.

Briefly, the method consists of placing the bronchoscope over the deformed carina and puncturing it with a needle designed for this purpose. The area is swabbed with alcohol and the needle with stylet in it is advanced through the carina about 5 to 8 mm. The stylet is withdrawn and the needle advanced slowly for 2 or 3 cm. with gentle aspiration. The needle is then withdrawn without aspiration and the puncture site swabbed with silver nitrate. If blood is aspirated the needle is removed immediately.

The contents of the needle and syringe are washed out with saline solution and the material placed in a formalin solution for pathologic examination in the usual manner.

During the past seven years, 83 patients were subjected to puncture of the carina by this method with "minimal risk or none at all." In 69 patients this was done as an aid in the diagnosis of a suspected bronchogenic carcinoma or a carcinoma of the middle or inferior thirds of the esophagus. Positive histologic data establishing a diagnosis of carcinoma was obtained in 26 patients. In some instances the histologic type of carcinoma was obtained.

The author believes that this method could be applied to other diseases such as mediastinal tumors, Hodgkin's disease, sarcoidosis and lymphogranulomas, but not to soft mediastinal tuberculous lymph nodes.—*Frank J. Rigos, M.D.*

DI GUGLIELMO, L., CITRONI, G. A., and CATTANEO, L. La ricerca e la valutazione dello spasmo bronchiale nella broncografia. (The investigation and evaluation of bronchial spasm in bronchography.) *Radiol. med.*, July, 1958, *44*, 609–619. (From: Istituto di Radiologia and Clinica Otorinolaringoiatrica, Università di Pavia, Pavia, Italy.)

This article is based on the large experience of Di Guglielmo, Pigorini and Citroni, whose excellent book "La Broncografia" was reviewed in the July, 1958 issue of this *Journal.*

The presence of bronchial spasms during bronchography is quite a common occurrence. Generally, they may be attributed to technical factors, such as: inadequate preparation of the patient, insufficient anesthesia, and irritation from the bronchoscope. However, if these factors can be excluded, the occurrence of bronchial spasms during bronchography should always be considered a pathologic manifestation.

The most common roentgen findings are: a narrowing or even a stenosis of a segment of a bronchus or of several bronchi; spasm involving the bronchus either for a very short distance, usually near its origin, or for all its length up to the peripheral branches which may appear dilated; concentric appearance of the stenosis with clearly outlined walls of the bronchus, unless an inflammatory process is associated with the functional manifestation. In a few cases one may observe the appearance of several spasms in a single bronchus, while in others the spasms extend to all the bronchi of a lobe or of more lobes and even of the entire lung. In this case the bronchi appear like long, thin lines without any evidence of the normal broncho-alveolar pattern, giving rise to a finding the authors have compared very aptly to "spider's legs."

The authors have observed these findings especially in cases of bronchial asthma. However, they point out that the presence of these findings alone does not warrant the roentgenologic diagnosis of bronchial asthma, because the same changes can be noted in cases of emphysema and of certain bronchitis. In bronchiectasis the presence of spasms assumes a great importance because it indicates that the muscular and elastic components of the wall of the bronchus are not deeply involved and, therefore, the pathologic process is still reversible. Furthermore, the presence of spasms in territories surround ing the bronchiectasis is of prognostic value because it signifies that the inflammatory process is progressing. Similar changes can be observed in abscess of the lung, tuberculosis and pneumoconiosis and they should be interpreted as functional alterations of territories of a lung apparently not involved by the disease. In cases of lung tumors the occurence of spasms during bronchography is generally due to an inflammatory process associated with the neoplastic lesion. Finally, in cases of chronic bronchitis when the inflammatory process has involved all the elements of the bronchial wall, there is no evidence of

spasms indicating, therefore, the irreversibility of the process.

The article contains many reproductions which illustrate very clearly the different roentgen findings.—*A. F. Govoni, M.D.*

Dickie, Helen A., and Rankin, John. Farmer's lung; an acute granulomatous interstitial pneumonitis occurring in agricultural workers. *J.A.M.A.*, June 28, 1958, *167*, 1069–1076. (Address: J. Rankin, 1300 University Ave., Madison 6, Wis.)

Farmer's lung is a potentially serious and crippling disease that results from handling a variety of dusty, moldy organic materials. The symptoms are shortness of breath, cough, weight loss, chills, fever and hemoptysis. This condition differs from silo-filler's disease in both causation and symptoms.

The roentgenographic appearance varies considerably with the severity and the duration. Extensive interstitial changes are sometimes seen, suggesting "azotemic lung." The usual finding, however, is a diffuse interstitial pneumonitis with varying degrees of patchy pneumonic densities. These more conglomerate densities tend to clear within a week or two, but the peribronchial accentuation will persist for a month or longer. A normal appearing chest roentgenogram does not exclude the diagnosis of Farmer's lung.

This report is based on 39 cases. Lung biopsies were done in 8, and 2 cases are described in detail. Histopathologic study revealed a granulomatous interstitial pneumonitis with epitheloid and giant cells. Repeated exposure was followed by recurrence. No causative organism was found. A given exposure induced the disease in some persons while leaving others unaffected. Individual hypersensitivity to molds or to their products seemed to be a decisive factor.

Antibiotic therapy is not primarily indicated. The essential treatment is for the patient to avoid repetition of the exposure.—*Cecil W. Ely, M.D.*

Read, Barbara. Rheumatoid lung. *Proc. Coll. Radiologists, Australasia*, Dec., 1957, *1*, 77–80. (From: The School of Radiology, R. P. A. Hospital, Sydney, N.S.W., Australia.)

The clinical and roentgenologic features of a case of rheumatoid lung disease are briefly reported. Roentgenologic findings in this case were caused by diffuse interstitial pulmonary fibrosis, complicated by terminal abscess formation.

Pleural changes in rheumatoid lung disease are more common than pulmonary lesions. There may be basal pleural reactions, larger effusions and chronic pleural thickening.

In 4 other cases of rheumatoid disease the changes in the lung were those of interstitial pulmonary fibrosis.

It is thought that identical appearances in the lungs are produced by diverse disease processes which have a common factor of antigen-antibody disturbance.—*Cecil W. Ely, M.D.*

Jepson, Ewart M., Rose, F. Clifford, and Tonkin, Richard D. Thoracic actinomycosis. *Brit. M. J.*, May 3, 1958, *2*, 1025–1027. (From: Westminster Hospital, London, England.)

The authors report two cases of thoracic actinomycosis. The first case had been diagnosed originally as possible pulmonary tuberculosis but at autopsy, seven years later, adrenal failure was found due to extensive amyloidosis as a result of long-standing thoracic actinomycosis. The second case was correctly diagnosed on the first hospital visit and successfully treated with a combination of prolonged penicillin and streptomycin therapy.

Common to both patients were pain (pleuritic and rheumatic), weight loss, peculiar appearance of the ribs, empyema from which *Actinomyces Israeli* was cultured, elevated sedimentation rate, and leukocytosis. They differed in that the first case had no fever, while the second case had fever on admission. The first case also had clubbed fingers, while the second case was disabled by pain in his shoulders. This latter case had a hemoglobin of 58 per cent.

The authors feel that this disease is caused by a synergism of *Actinomyces Israeli* with another aerobe and requires trauma or a locally reduced resistance to produce a lesion. They emphasize the diagnositc importance of a characteristic osteitis seen on the chest roentgenogram. In the vertebrae, this consists of irregular rarefaction surrounded by osteosclerosis and in the ribs the same finding is associated with periosteal elevation. They suggest that treatment with penicillin and streptomycin is beneficial but, in some cases, it has to be extended over a long period of time.—*P. B. Parsons, M.D.*

Schulze, W. Röntgenologische Studien nach Aspiration von metallischem Quecksilber. (Roentgen studies after aspiration of metallic mercury.) *Fortschr. a. d. Geb. d. Röntgenstrahlen u. d. Nuklearmedizin*, July, 1958, *89*, 24–30. (From: Medizinische Universitätsklinik, Leipzig, Germany.)

This is a case report of a patient who attempted suicide by swallowing metallic mercury. She soon began to vomit and while so doing, she choked and aspirated a part of the metal. Manifestations of mercury poisoning disappeared within two weeks and under symptomatic treatment, the patient became well enough to be discharged from the hospital in about six months.

The initial roentgenogram, at the time of inhalation of the mercury, showed fine metallic densities in both lungs, more in the right. The patient was

followed over a five year period. It was noted that the metallic particles shifted more and more to the periphery of the lungs, and became fewer in number. No toxic effects have been noted.—*Samuel Richman, M.D.*

SAXTON, JOHN. Lobar emphysema in a baby. *Proc. Coll. Radiologists, Australasia*, Dec., 1957, *1*, 71–74. (From: The School of Radiology, R.P.A. Hospital, Sydney, N.S.W., Australia.)

This condition is of particular importance to radiologists because they alone can make the positive diagnosis of the acute respiratory emergency.

The case of a five week old infant with intermittent respiratory distress for three weeks is reported. Roentgenologic findings of obstructive emphysema of the left upper lobe and compression of the left lower lobe were observed. Also some compression of the right upper lobe and a compensatory emphysema of the right lower lobe were noted. No mediastinal swing was found at fluoroscopy. A left upper lobectomy was performed the following day with removal of a huge overdistended lobe which showed no other pathology.

The author refers to this as "congenital lobar emphysema" but admits that the congenital etiology is not well established. The exact cause has never been determined although several have been suggested. The condition has never been reported in either lower lobe.

Lobar emphysema should be suspected when a normal afebrile infant begins to have attacks of dyspnea with or without cyanosis. Chest roentgenography and fluoroscopy show typical obstructive emphysema of one portion of one lung with compression of the remaining part of the same lung. Other conditions to be considered are agenesis of one lung, pneumothorax, mucoviscoidosis and diaphragmatic hernia, but these offer little difficulty in the differential diagnosis.—*Louis C. Lippert, M.D.*

MOKROHISKY, JOHN F. So-called "Meigs' syndrome" associated with benign and malignant ovarian tumors. *Radiology*, April, 1958, *70*, 578–581. (Address: St. Vincent's Hospital, Green Bay, Wis.)

The author reviews the clinical syndrome of benign fibroma of the ovary associated with ascites and hydrothorax in which the effusions disappear following removal of the ovarian tumor. This entity was described by Meigs and Cass in 1937 and have since been called the "Meigs syndrome." It is less well known that the syndrome also occurs with malignant ovarian neoplasms and removal of these tumors may result in disappearance of the effusions. It is a relatively uncommon occurrence either with a benign or a malignant tumor.

Meigs recently redefined this syndrome and included thecomas, granulosa cell tumors, and Brenner tumors as well as fibromas as being the tumors most commonly associated with this clinical picture. Meigs also listed 14 cases of malignant ovarian tumors which produce similar findings; most of these tumors were papillary cystadenocarcinomas, with one Krukenberg tumor, a fibrosarcoma of the ovary, and an adenocarcinoma of the round ligament.

The author presents 2 cases of the syndrome, one due to a fibroma of the ovary and the other to a bilateral cystadenocarcinoma of the ovary. In both cases, the effusions disappeared following removal of the tumor. In his opinion, the associated ascites and hydrothorax may not indicate secondary metastatic implants of peritoneum or pleura and thus it is important to recognize the benefits of surgical removal of the tumor, whether benign or maligant.—*John S. Alexander, M.D.*

LEMAHIEU, S. F., LAMIROY, H., and PANNIER, R. (Bruges, Belgium.) Manifestations pulmonaires des chorio-carcinomes. (Pulmonary manifestations of choriocarcinomas.) *J. belge de radiol.*, 1958, *41*, No. 2, 195–220.

Choriocarcinoma is propagated by the blood and appears at a distance, in this way acting like sarcoma rather than carcinoma with its lymphangitic spread. There is a predilection for the lungs, more than one-half of the metastases being pulmonary.

Three types of lesions are identified which are the same roentgenologically but differ in their pathogenesis: (1) True metastases which develop independently of the primary focus; (2) ectopic lesions from the benign mole which can disappear when the primary focus is removed; and (3) transformations *in situ* where a benign trophoblastic lesion becomes malignant in the lungs.

Pulmonary lesions appear early, usually several weeks after discovery of the primary tumor. They are silent like other metastases, except for the frequent occurrence of hemoptysis.

Roentgenologically, on the one hand it is necessary to be suspicious of an atypical picture of "tuberculosis" in a female who is or has been through a somewhat abnormal pregnancy. On the other hand, all pulmonary lesions in a known choriocarcinoma must not automatically be considered metastatic.

Three groups of roentgenologic patterns are distinguished: solitary, multiple macronodular, and multiple micronodular densities. One of these patterns may change into another during the course of the disease. There may also be a complicating pleural reaction. The macronodular "bronchopneumonic" pattern is most frequent, the miliary is least often seen. In the first type, there is a large single parenchymal density, perhaps with compression of the adjacent lung or associated segmental atelectasis. The mass grows rapidly in size. The second type includes multiple macronodular opacities, more or less

round and hazy. These are predominantly at the bases. The pattern is more suggestive of bronchopneumonia than of sarcoma. The third type consists of micronodules not over 3 mm. in size. Sometimes there are also linear densities resulting in a reticulogranular pattern. The appearance may be "pure" miliary or may resemble a lymphangitic spread. Finally, the choriocarcinomatous tissue may be strictly confined to the lumen of a pulmonary artery with no parenchymal invasion. Thrombosis of the endarteries may give a reticulogranular appearance to the lung particularly at the base with or without infarction.—*Marcy L. Sussman, M.D.*

Fontaine, R., Warter, P., Franck, P., Kim, M., and Wagner, R. Contribution à l'étude radiologiques des opacités médiastinales. (Contribution to the radiologic study of mediastinal opacities.) *J. de radiol., d'électrol. et de méd. nucléaire*, June–July, 1958, *39*, 349–357. (From: Clinique Chirurgicale A, Strasbourg, France.)

Many mediastinal diseases have a silent course, but are detected through systematic roentgenologic investigations.

The 11 selected cases reported here show that while the location of mediastinal masses is easy, it is often difficult to determine their exact origins. This is because the area contains respiratory, cardiovascular, lymphatic, endocrine, digestive and nervous structures. Therefore, one may need to use many of the available techniques which include fluoroscopy, plain roentgenography performed at various angles, opacification of the esophagus with barium, bronchography, kymography, pneumoperitoneum, pneumothorax, angiocardiography, cervical phlebography and laminagraphy.

The newest technique is pneumomediastinography; when combined with laminagraphy it often outlines the site, form, dimensions and anatomic extension of the tumor.

The correct diagnosis can usually be reached by properly choosing from among these techniques.—*Frank A. Riebel, M.D.*

Shamma's, Munir H., and Benedict, Edward B. Esophageal webs; a report of 58 cases and an attempt at classification. *New England J. Med.*, Aug. 21, 1958, 259, 378–384. (From: The Medical and Surgical Services, Massachusetts General Hospital, and the Departments of Surgery, Harvard Medical School, Boston, Mass.)

This study is an analysis of 58 cases at the Massachusetts General Hospital and the Massachusetts Eye and Ear Infirmary, with an attempt at classification. In 48 of these patients the webs were in the upper third of the esophagus, 2 were in one patient with one each in the upper and middle thirds, 4 were in the lower third, and 4 were associated with benign mucous membrane pemphigus (location not indicated). The upper esophageal webs were further classified as 23 with anemia, 14 without anemia, and 12 with no hematologic data.

Of the 48 patients with upper third webs, 23 fit the descriptions of the Plummer-Vinson syndome in the literature. All 23 were in women between the ages of 30 and 75, and all had hypochromic anemia with hemoglobin levels ranging from 3 to 11.8 gm. Blood smears of 16 of these patients showed varying degrees of anisocytosis, poikilocytosis and hypochromia. A red smooth tongue with atrophic papillae was found in 14 (61 per cent). The duration of the dysphagia in 21 patients varied from 4 months to 46 years or more. The association of esophageal webs with carcinoma, and with thyroid disease is discussed. In 9 patients (about 16 per cent) carcinoma developed, 6 in the buccal mucosa and 3 in the esophagus. Disease of the thyroid was present in 7 patients, 4 with myxedema and 3 with nodular goiter. One of the latter was toxic, and two nontoxic.

Tables are included showing in detail the relative occurrence of the various findings.—*D. S. Kellogg, M.D.*

Abdomen

Kallenberg, A., and Mohr, K. Darstellung von Fisteln und Perforationen mit einer wässerig suspendierten mikrokristallinen Kontrastsubstanz. (Demonstration of fistulas and perforations with a watery suspended microcrystalline contrast substance.) *Röntgen-Blätter*, June, 1958, *11*, 161–169. (From: Chirurgische Universitätsklinik, Köln, Germany.)

Study, over a period of years, concerning perforations of the stomach and duodenum has yielded, according to the authors, several basic facts, among which are:

(1) In patients with a potentially perforating gastric or duodenal ulcer a definite relationship exists between subsequent perforation and barium examination of the stomach. It is theorized that in patients who have been on an ulcer diet, the sudden distention of the stomach with a large amount of barium-water suspension critically stretches the thinned-out, ulcerated gastric or duodenal wall, leading to perforation. Outside influences such as manual palpation and compression are almost never of importance in the genesis of perforation which often does not occur until twenty-four hours after the barium meal examination.

(2) There is a definite difference between perforation of the stomach and of the duodenum. Experimental perforation distal to the pyloric ring results in continual spasm of the pyloric muscle so that for

a long period of time gastric contents do not pass into the perforated duodenum. Such is not the case, of course, in perforated gastric ulcer.

Although it is clinically desirable to demonstrate perforations and fistulas of the stomach and duodenum roentgenologically, their demonstration has been restricted because of the type of contrast medium employed for such purposes. Barium sulfate in particular is objectionable because of the severe foreign body reaction it stimulates in the peritoneal cavity. Watery contrast media thus far employed for upper gastrointestinal opacification have had the following disadvantages: (1) Disagreeable taste; (2) unsatisfactory demonstration of mucosal details, somewhat improved by the addition of an emulsifying agent such as carboxymethylcellulose to the watery medium; (3) short absorption time of watery iodine-containing contrast media often leads to a hasty examination; (4) egress of such media into the pleural or peritoneal cavity causes intense pain, and because of the lack of isotonicity an irritative reaction of the serosal surface of the peritoneum or pleura results.

The authors devised an isotonic watery contrast suspension (n-propylester, 3, 5, diiodo-4-pyridon-N-acetic acid) which in microcrystalline form in concentration of 50 per cent contains 30 per cent iodine. Benzyl alcohol is added for sterility and carboxymethylcellulose for proper viscosity. This material when present outside the alimentary tract, *e.g.* in the peritoneal cavity, is absorbed slowly, about 95 per cent of the material disappearing in seventy-two hours. The medium within the alimentary tract passes through the canal in the same manner as barium sulfate.

Numerous examinations employing this new medium have convinced the authors that it provides contrast similar to barium sulfate without the disadvantages of the simple watery iodine-containing contrast media.

Interesting illustrative cases show the use of the new medium in patients with ulcerative and operative perforation of the stomach and duodenum. The particular value of the medium in the evaluation of the acute abdomen is stressed.—*Harold E. Fulton, M.D.*

LEE, HERBERT C., and KAY, SAUL. Primary polyarteritis nodosa of the stomach and small intestine as a cause of gastro-intestinal hemorrhage. *Ann. Surg.*, May, 1958, *147*, 714–727. (From: The Departments of Surgery and Surgical Pathology, Medical College of Virgina, Richmond, Va.)

The authors report two cases of polyarteritis nodosa of the stomach and small intestine, one with primary and solitary involvement of the stomach, and the other affecting the stomach and jejunum. A third case was diagnosed as necrotizing thrombophlebitis of the mesenteric veins accompanied by gangrene of the ileum and jejunum. The diagnosis in each case was made following surgery for gastrointestinal bleeding or acute abdominal pain.

The first case has had no subsequent symptoms for eighteen months, the second case for six months, and the third case for seven years. The first case had arrested pulmonary tuberculosis, and the second rheumatoid arthritis. Both had been treated with many medications, including penicillin and cortisone. The previous history in the third case was irrelevant.

The first and second cases showed involvement of the arteries, while in the third case there was involvement of the veins only. The relationship of allergy as a cause of polyarteritis nodosa was not consistent with the medical history in the three cases. There were no specific roentgen diagnostic signs.—*P. B. Parsons, M.D.*

REED, EDSEL S., WILLARD, JOHN H., and WELLS, PAUL O. Multiple benign gastric ulceration; report of two unusual cases. *Radiology*, April, 1958, *70*, 564–569. (Address: E. S. Reed, Harlan Memorial Hospital, Harlan, Ky.)

The authors report two unusual cases of multiple and simultaneous benign gastric ulcers.

One patient, a thirty-two year old female with a known duodenal ulcer, was seen because of failure to respond to medical management. The gastrointestinal examination revealed the presence of two apparently benign gastric ulcers on the greater curvature, as well as the previously identified duodenal ulcer adjacent to the pylorus. A subtotal gastrectomy was performed and subsequent examination of the surgical specimen revealed all three ulcers to be benign. The other patient, a sixteen year old male with a two-year history of drinking one pint of whiskey weekly, was seen because of epigastric pain, nausea and vomiting. There was no history of hematemesis or melena. An examination of the upper gastrointestinal tract revealed the presence of four separate gastric ulcers in the antral region of the stomach. The patient responded well to intensive medical management with complete healing within a month.

A review of the published reports of benign and malignant gastric ulcers indicates that ulcerations of the greater curvature represent from 1 to 9 per cent of all benign gastric ulcers, while the incidence of malignant ulcers in that location varies from 20 to 100 per cent, with an average of about 50 per cent. These figures are in contrast to the previous contention that ulcers in this location are almost universally malignant. However, it is still generally agreed that all ulcers in this location should be resected. Although multiple ulcerations in other locations are not common, the simultaneous occurrence of two or more ulcers apparently does not add to the likelihood

of malignancy. The authors therefore suggest that in benign appearing multiple ulcerations, other than greater curvature ulcers, a period of therapeutic trial under close observation seems justifiable.—*Edward B. Best, M.D.*

Brown, Charles H., and Strittmatter, William C. Obstructive lesions of the duodenum distal to the bulb. *Radiology*, May, 1958, *70*, 720–727. (Address: C. H. Brown, Cleveland Clinic, Cleveland 6, Ohio.)

The authors present a review of the causes of postbulbar duodenal obstruction illustrated with representative roentgenograms from their own cases.

The duodenum, because of its relative fixation and proximity to numerous structures, is subject to many lesions which may produce either partial or complete obstruction. These lesions may be grouped in three major categories: congenital or developmental, extrinsic, and intrinsic. Congenital or developmental lesions may affect any portion of the duodenum. The obstructive causative factor may be pressure from a superior mesenteric artery, congenital bands, volvulus, malrotation or an annular pancreas. Extrinsic or extraduodenal obstruction may be caused by pressure from cysts or tumors or enlargement of any of the adjacent structures, usually with widening of the duodenal loop. This widening must be correlated with the patient's habitus since the "steer horn" stomach also is associated with a wide duodenal loop. Obstruction due to intrinsic or intra duodenal disease is usually the result of either ulceration or neoplasm. However, the authors warn that in many cases, especially those in which the lesion occurs in the region of the ampulla of Vater, it is impossible to roentgenographically distinguish intrinsic from extrinsic disease.—*Edward B. Best, M.D.*

Fleischner, Felix G., and Mandelstam, Paul. Roentgen observations of the ileostomy in patients with idiopathic ulcerative colitis. II. Ileostomy dysfunction. *Radiology*, April, 1958, *70*, 469–480. (Address: F. G. Fleischner, 330 Brookline Ave., Boston 15, Mass.)

Ileostomy dysfunction is a constant threat to patients with an ileal stoma. Numerous complications of ileostomy may occur, including major skin excoriations, wound dehiscence, fistulas, prolapse and retraction. Another serious and sometimes fatal complication is the syndrome of obstruction with prestomal ileitis and fluid and electrolyte imbalance, termed "ileostomy dysfunction" by Warren and McKittrick. They reported this syndrome in 62 per cent of their patients.

The presence of a few moderately dilated, gas- and fluid-filled loops of bowel, best seen with the patient erect, is quite common in ileostomy dysfunction. The classical picture of a high degree of small-intestinal obstruction is rather rare. Barium studies reveal marked widening of the prestomal ileum, with a diameter ranging from 4 to 10 cm. Kerkring's folds, if present at all, are shorter, wider, and more widely spaced than normal. Gross small-intestinal transit time in orally administered barium is markedly prolonged.

Barium enema through the ileostomy is the most helpful examination for the detection of ileostomy dysfunction. It reveals the presence of widening of the terminal ileal loop, the presence of large amounts of retained fluid, and the absence of Kerkring's folds. Obstructive narrowing at the cutaneous or subcutaneous level of the ileostomy is also demonstrated.

The histories of 5 patients with severe ileostomy dysfunction are presented. The etiology of this abnormality and measures for its prevention and alleviation are discussed.—*Arno W. Sommer, M.D.*

McCort, James J. Ascaris ileus in children. *Radiology*, April, 1958, *70*, 528–531. (Address: Santa Clara County Hospital, San Jose, Calif.)

Obstruction of the intestinal tract by a coiled mass of mature *Ascaris lumbricoides* is a rare but serious occurrence in infancy and childhood. When large numbers of mature worms migrate from their usual habitat in the jejunum, they may form a bolus which will cause obstruction of the intestine and if not recognized early, may go on to cause necrosis, perforation, peritonitis and death.

The life cycle of *Ascaris lumbricoides* is briefly described as is some of the epidemiology. Two stages in the life cycle of the worm may produce symptoms: (1) the larval stage, when invasion and inflammation take place in the lung alveoli; (2) the adult stage, when worms lodge in the small bowel where toxins are liberated, causing systemic reactions. Invasion of the common duct has been known to cause jaundice, and invasion of the pancreatic duct can cause pancreatitis.

Various authors who have contributed to the roentgenographic description of this condition are mentioned.

The following four roentgen signs are noteworthy: 1. (a) with barium study, a cylindric filling defect in the jejunum and (b) a string-like shadow representing the barium-filled enteric canal of the parasite (Archer and Peterson); 2. (a) linear parallel shadows due to adherence of barium to the outside of the worm and (b) disordered small bowel motility (Strong and Warrich). Occasionally, a plain roentgenogram of the abdomen will show a mass of worms in a distended segment of intestine. Medical purge is usually sufficient treatment, but surgery is occasionally required in complicated cases.

Two cases of Ascaris ileus occurring in four year

old children are presented along with roentgenographic reproductions to illustrate this unusual condition.—*Z. Petrany, M.D.*

MUJAHED, ZUHEIR, and EVANS, JOHN A. Gas cysts of the intestine (pneumatosis intestinalis). *Surg., Gynec. & Obst.*, Aug., 1958, *107*, 151–160. (From: The Department of Radiology, The New York Hospital-Cornell Medical Center, New York, N. Y.)

Pneumatosis intestinalis is a relatively rare disease with only 255 patients reported in the literature up to 1952. This disease is quite frequent in pigs and less common in other animals.

In humans the gas filled cysts vary in size from a few millimeters to several centimeters and may be found in the stomach, small intestine, colon or mesentery. Occasionally the cysts may perforate and give rise to free air in the peritoneal cavity. The cysts are predominantly mucosal and submucosal in infants and subserosal in adults. The condition is most frequent in the middle age group, but can be found in infants and in the a ed. In infants the disease may cause an intractable diarrhea. In adults it may be asymptomatic or it may cause a partial obstruction, volvulus of the intestine, adhesions or tension pneumoperitoneum. In more than half of the patients it is associated with other lesions of the gastrointestinal tract such as gastric or duodenal ulcers, usually of the stenotic type.

The mechanical theory explains the formation of these gas filled cysts better than any other theory. It presupposes a break in the continuity of the mucosa and then the gas being forced into the submucosa or subserosa forms cyst-like collections. The mucosal defects heal over and the cysts may at times have a flat endothelial layer. Microscopically a nonspecific inflammatory reaction is present.

Pneumoperitoneum without the clinical picture of perforation and peritonitis should point to this disease as a possibility.

Gas cysts of the mesentery may be suspected on a scout film when bizarre relatively fixed mid-abdominal gas collections are seen that do not conform to the pattern of intestinal gas.

Some intestinal and colon examinations will reveal cyst-like gas collections to be outside the intestinal tract when they are located in the mesentery. Intramural cyst-like gas collections will be revealed as sharply marginated polyp-like defects that may cause various degrees of obstruction. When there is small bowel involvement there may be interposition of a loop of bowel between the liver and the diaphragam called Chilaiditi sign.

This condition must be differentiated from emphysematous gastritis and intestinal emphysema of the stomach, and advanced ulcerative colitis. The authors report 7 patients with this disease: 4 were in infants with diarrhea and 3 were in adults. Roentgenographic studies were done on the adults, establishing the diagnosis. It was confirmed in 2 of these 3 patients.—*Frank J. Rigos, M.D.*

BARNHARD, HOWARD J., and HIDY, W. DEAN. Intraluminal mesentery as cause of small-bowel obstruction. *Radiology*, April, 1958, *70*, 574–577. (Address: University of Arkansas Medical Center, Little Rock, Ark.)

The authors describe a unique case of intermittent partial small bowel obstruction due to the intraluminal location of a segment of small bowel mesentery. No similar case has been recorded.

The patient, a twenty-six year old colored male, was hospitalized for intestinal obstruction. After appropriate decompression, the patient improved and diagnostic studies were continued. Six days after a barium meal he was found to have several barium-filled loops of small bowel situated in the left lower abdomen. These loops presented irregular filling defects with a tendency to long folds parallel to the bowel walls. A resection of a portion of the distal ileum was performed. Examination of the specimen revealed the intraluminal presence of a 15×8 cm., slightly necrotic, mesenteric remnant which entered the bowel through an ulcer on the mesenteric side.

Since this case likely represents a new entity, its etiology is not definitely established. Several mechanisms are possible which include: (1) spontaneous intrusion of a portion of mesentery following a bowel perforation; (2) invagination of a Meckel's diverticulum, with its own small mesentery and subsequent sloughing of its wall; (3) intussusception of the small bowel followed by autoamputation and autoanastomosis with persistence of a large portion of the intussuscepted mesentery. The authors exclude the first two possibilities and justify the latter mechanism by virtue of the size of the mesenteric remnant and that it entered the bowel through an ulcer on the mesenteric side. It is conceded that the intussusception may have been initiated by a Meckel's diverticulum in view of the location of this process in the distal ileum.—*Edward B. Best, M.D.*

FLEISCHNER, FELIX G., and SAYEGH, VICTOR. Assessment of the size of the liver; roentgenologic considerations. *New England J. Med.*, Aug., 1958, *259*, 271–274. (From: The Department of Radiology, Beth Israel Hospital, and Harvard Medical School, Boston, Mass.)

The size of the liver is often difficult to evaluate by palpation or by plain roentgenography. Accurate determination of the size of the liver must take into account the position of the diaphragm and constitutional variations in the shape and position of the liver.

Certain facts are well known that increase our knowledge of the variability of the position of the

normal liver. Roentgenography has determined how variable the position of the gallbladder may be depending upon the body habitus, and this in turn reflects corresponding variations of the liver. The relationship between body build and the shape and topography of the liver is mentioned in textbooks of anatomy, physical diagnosis and roentgenology; however, these general statements are of little help in the individual patient.

Roentgenologic attempts at determining the hepatic size are not satisfactory for application in routine clinical work. All procedures are too cumbersome, expensive or possibly dangerous.

The authors have found that an enveloping line drawn around the biliary tree as visualized by direct cholangiography with projections in sagittal and lateral roentgenograms gives a fair appraisal of the size and shape of the liver.

Fifty consecutive patients with complete records were analyzed in this manner and 3 measurements recorded: (1) the extent of the liver to the left; (2) the lower liver edge which forms an angle of less than 42° to 60° with the horizontal; and (3) on the lateral roentgenogram the height of the posterior hump of the liver, that is, the area of contact with the posterior abdominal wall.

The impression was gained that the edge of the right lobe of the liver that extended far over to the left was high and had a gentle slope between 22° and 42°. In livers that were entirely on the right side, the right lobe extended far down and the lower edge had a steep slope of 48° to 60°. Topographic arrangement and shapes of the liver varied and were closely associated with different phenotypes. In short plump subjects with wide transverse and sagittal diameters, the liver extended far to the left with an angle of 42° or less and a large area of posterior abdominal wall contact. Slender individuals with short transverse and sagittal diameters had a liver that extended to the midline or less with an angle of 48° to 60° and a short area of posterior abdominal wall contact.

Another study was made using abdominal roentgenograms taken in the prone position, as routinely taken two hours after a barium meal and after evacuation in colon examinations. The level of the edge of the right lobe of the liver was related to the anterior costal margin or the iliac crest. A group of 120 patients with presumably normal livers was studied and the relationship between the downward extension and the lower liver edge noted. In subjects with a slope of the liver edge of less than 42° the liver edge in 95 per cent was at, or 1 fingerbreadth below, the costal margin. Among the subjects with a steep slope of the liver edge, there was about an even distribution in the downward extension of the liver reaching 1 to 4 fingerbreadths below the costal margin.

From these studies it is clear that in determining the size of the liver either by physical examination or by roentgenography, greater attention must be paid to the body type of the subject and slanting edge of the liver in order to avoid the error of misjudging, usually overestimating, the size of the liver. —*Frank J. Rigos, M.D.*

Leger, Lucien; Boquien, Yves; Kerneis, J.-P.; Guyet, Paulette; and Hautefeuille, P. Dysgénésies congénitales complexes des voies biliaires intra-hépatiques au cours des cirrhoses juvéniles avec hypertension portale. (Complex congenital dysgenesis of the intrahepatic biliary passages in the course of juvenile cirrhosis with portal hypertension.) *Presse méd.*, June, 1958, *66*, 1147–1151. (From: Hôpital de Créteil, et Clinique médicale B du Centre hospitalier régional de Nantes, Nantes, France.)

Two cases of juvenile cirrhosis with portal hypertension are reported. The first case, sixteen years of age, was first seen at the age of ten with a gastrointestinal hemorrhage. Development was retarded; the liver was large and the spleen palpable. There followed recurrent bleeding episodes during the next six years with violent abdominal pain. Liver function tests were negative except for a positive cephalin-cholesterol test. Gross esophageal varices were demonstrated roentgenologically. Liver biopsy showed an advanced sclerosis of the hepatic parenchyma. Splenoportography (confirmed later by autopsy) showed two venous systems leaving the spleen. One followed a normal path visualizing an intact portal trunk and a slender intrahepatic branch. There was also a collateral circulation to the perisplenic and gastric coronary systems. The other consisted of a large vein which, after leaving the hilus, described a U curve in front of the spine and entered the inferior vena cava, constituting a spontaneous portacaval shunt. The splenic pressure was greatly increased to 58 cm. of water. Subhepatic catheterization demonstrated a wedge pressure of 22 mm. Hg as against 5 mm. in the inferior vena cava. Hepatic clearance tests gave K BSP=0.11, essentially normal; K Au^{198}=0.11, much decreased; and

$$\frac{\text{K BSP}}{\text{K Au}^{198}} = 1,$$

much increased. This indicates that there is little cellular change but an important injury to the Kupfferian system or the hepatic circulation unless these changes are the result of pre-existing anastomoses. A termino-lateral portacaval anastomosis was performed. The child died twelve days later.

The second case was that of a female, twenty-one years of age, five and one-half months pregnant. The principal complaint was hematemesis and melena. The liver was moderately enlarged; the spleen was not palpable. The liver function tests were normal. Delivery occurred normally but was followed in two days by gastrointestinal bleeding. Several such episodes occurred during the following

month. Splenomanometry gave a pressure of 36. The splenic vein was very dilated and tortuous, being almost as large as the portal trunk. The gastric coronary vein was dilated. Subhepatic wedge pressure was 20 mm. Hg. At surgery, the liver was large and smooth with a whitish covering. The spleen was removed and a termino-lateral splenorenal anastomosis performed. The left kidney was nodular; biopsy showed polycystic kidney which subsequent urography proved to be bilateral.

In the first case, the autopsy revealed a nodular hypertrophic cirrhosis which on section showed a number of rosary-like cavities containing bile. They seemed lined by a biliary-type epithelium and represented huge biliary canals. They communicated with each other and with the biliary trunk. The condition was diagnosed as a congenital dysplasia. In the second case, the liver biopsy showed a portal sclerosis. There were large abnormal biliary passages, some appearing cystic. The condition was interpreted as a complex dysplasia of the intrahepatic bile passages.

According to the authors, the two reported cases represent juvenile cirrhosis of the liver with multiple dysgenesis. Comparison is made with other cases in the literature.—*Marcy L. Sussman, M.D.*

JORPES, ERIK, MUTT, VIKTOR, TOMENIUS, JOHN, and BACKLUND, VIDAR. Cholecystokinin in roentgenologic examination of the biliary tract. *Röntgen-Blätter*, May, 1958, *11*, 145–157. (From: Karolinska Institutet, Chemistry Department II, St. Göran's Hospital, Medical Policlinic I and Central Roentgen Department, Stockholm, Sweden.)

Cholecystokinin, a hormone of the duodenal mucosa which causes contraction of the gallbaladder, was discovered by Ivy and Oldberg in 1928. They ascribed the action of their secretin preparation on the gallbladder to a specific hormone, cholecystokinin, which accompanies the secretin and supplements its action in hormonal stimulation of the digestive functions. In the past five years purified preparations of secretin and pancreozymin-cholecystokinin have been made available for clinical use. Preparations of cholecystokinin corresponding to 0.04 mg. of substance per kg. of body weight, a total of 3 mg. in adults, were injected intravenously in 650 cases in connection with cholecystography, by the authors. There were no toxic effects from the cholecystokinin preparation.

The authors in expectation of finding a more rapid and more effective means of emptying the gallbladder and visualizing the bile ducts at cholecystography, substituted the cholecystokinin test for the ordinary egg-yolk meal in a series of patients. These patients were examined twice, for comparison of the customary technique after an egg-yolk meal with that in which evacuation is produced with the help of intravenously injected cholecystokinin. This series consisted of 59 patients: 35 normal cases, 16 with gallstones, and 8 in which the gallbladder did not contract after either stimulant (considered pathologic by the authors).

Some facts inferred from the comparative study are:

(1) The degree of visualization of the bile ducts and the contraction of the gallbladder are not parallel in the two techniques. Four cases in which no contraction occurred after the egg-yolk meal reacted by contraction to cholecystokinin.

(2) In 23 cases the bile ducts were visualized better after cholecystokinin injection than after the egg-yolk meal; in 10 cases as well; in two cases not as well.

(3) In 14 cases the gallbladder contracted better after cholecystokinin than with the egg-yolk meal; in 16 cases as well; in 5 cases not as well.

(4) Cholecystokinin is seen to be uniformly superior with respect to rapid onset of contraction of the gallbladder (1–2 minutes) and the maximum degree of contraction of the gallbladder (10–20 minutes). The egg-yolk meal gives a wide range of variations of onset of contraction and far slower reactions.

(5) Pylorostenosis does not interfere with the effect of cholecystokinin as it does with fatty meals.

(6) In general, the cholecystokinin test reduces the time necessary for cholecystographic examination of the gallbladder and bile ducts to one-fourth of that required by the egg-yolk meal technique.

(7) Barium examination of the stomach can be performed within a short time after the examination of the biliary tract.

(8) The use of secretin and cholecystokinin in succession offers the possibility of analyzing the pancreatic juice and bile separately, when collected through a duodenal tube. Since these secretions are not contaminated with digestive products, they can be analyzed for normal components and for the presence of leukocytes, bacteria, and cancer cells.—*Harold E. Fulton, M.D.*

SCHULTZ, E. H., JR. An aid to the diagnosis of pneumoperitoneum from supine abdominal films. *Radiology*, May, 1958, *70*, 728–731. (Address: 330 Mt. Auburn St., Cambridge 38, Mass.)

Upright roentgenograms of the abdomen, demonstrating free air in a subdiaphragmatic location, remain the best means for the roentgenologic diagnosis of pneumoperitoneum. Sometimes, however, only roentgenograms in the supine position are available for study. In these cases, and in the unusual instances of obliteration of the subdiaphragmatic space, diagnosis of pneumoperitoneum is still possible by detecting the serosal surface of the bowel outlined by intraperitoneal gas. The value of this

sign is illustrated by a case report where free peritoneal gas failed to ascend to the subdiaphragmatic space in the upright position.

It was Rigler's original impression that this roentgen sign, a visible outer bowel surface, is usually demonstrated only in the presence of relatively large amounts of peritoneal gas and fluid. The author, using both clinical material and laboratory animals, has substantiated this view. He reports also that the bowel wall can be visualized with large amounts of peritoneal air alone, but that much less air is required to produce this sign when a moderate amount of peritoneal fluid is present. The presence of fluid apparently causes the gas filled loops of bowel to float to the surface and separate, which allows the air-bowel interface to be more nearly parallel to the roentgen rays.

The author also observed that the falciform ligament was outlined by gas contrast on the roentgenograms of both laboratory animals and on the supine roentgenogram of one patient. He suggests that its identification on supine roentgenograms would seem to be of equal significance to the other roentgen signs of free peritoneal gas.—*Edward B. Best, M.D.*

Genitourinary System

Dihlmann, W. Vergleichende Untersuchungen über den Wert der intravenösen Kompressionsurographie. (Comparative studies regarding the value of compression in intravenous urography.) *Fortschr. a. d. Geb. d. Röntgenstrahlen u. d. Nuklearmedizin*, July, 1958, *89*, 104–108. (From: Röntgenabteilung der Medizinischen Universitätsklinik, Rostock, Germany.)

The author performed comparative studies to determine the value of compression in intravenous urography. A rubber balloon held by a cloth band was placed above the symphysis pubis and after 2 cc. of the contrast medium was injected intravenously the balloon was inflated. A roentgenogram was taken eight minutes after the beginning of the injection. Just before taking the second roentgenogram at eighteen minutes, the balloon was removed.

Two hundred studies were done with and 200 without compression, all on normal subjects.

The author believes that by the use of subrapubic compression, a better and more complete visualization of the urinary tract is obtained. Compression doubles the chances of complete filling of the renal collecting system and, in addition, increases the number of times the ureters may be visualized.—*Samuel Richman, M.D.*

Galdini, Salvatore, and Cirla, Augusto. Considerazioni cliniche e radiologiche su quarantatrè casi di tumori renali. (Evaluation of the clinical and radiological findings in forty-three cases of tumors of the kidney.) *Radiol. med.*, July, 1958, *44*, 643–662. (From: Divisione Chirurgica and Istituto di Radiologia, Ospedale S. Anna ed Uniti L.L.P.P., Como, Italy.)

The diagnosis of a neoplastic process of the kidney is in a certain number of cases quite difficult to make. It is in such cases that the radiologist has to use all his experience and to take recourse to several different roentgenologic investigations in order to arrive to the correct diagnosis.

The authors review 43 cases of tumors of the kidney, all verified. The age of the patients varied from two to seventy-eight years, the most frequent incidence being in the sixth and seventh decades. There were 34 males and 9 females.

Histologically, the most common were the typical renal epithelioma (15 cases) and the hypernephroma (13 cases).

The roentgen findings are analyzed and discussed. The methods used for examination consisted of the standard roentgenologic procedures, laminagraphy and retroperitoneal air insufflation.—*L. F. Govoni, M.D.*

Gordon, I. R. S. Renal puncture. *J. Fac. Radiologists*, April, 1958, *10*, 108–112. (From: Department of Radiodiagnosis, United Bristol Hospitals, Bristol, England.)

The purpose of this paper is to describe a method of investigation of space-occupying lesions of the kidneys. This method is of value where urography reveals evidence of displacement and deformity of the calyces of a kidney, without giving satisfactory proof as to the nature of the lesion. It may not be desirable to perform an exploratory operation, and arteriography may merely demonstrate the existence of a space-occupying lesion without disclosing its nature.

Following the usual preliminary preparation for excretory urography, an intravenous injection of sodium diatrizoate is given. The patient is then put in the prone position, and a marker made up of lead shots at 1 cm. intervals is strapped to the patient's back, lying approximately over the pelvis of the kidney in question. Posteroanterior and lateral roentgenograms of the kidney are made to localize the point on the skin at which puncture is to be made. This point should be vertically above the center of the space-occupying lesion. After determining the approximate depth of the lesion, under local anesthesia a No. 22 gauge needle 15 cm. long is introduced. Injection of a few cc. of sodium diatrizoate will afford a roentgenographic record of the nature of the lesion and its location. If blood is withdrawn following puncture, it is assumed that the lesion is probably neoplastic, and no injection should be made because of the danger of disseminating tu-

mor cells. If clear fluid is obtained, the lesion is presumably cystic. If no fluid is obtained the needle was not placed correctly, or it may be in normal tissue.

Following injection of a contrast material, a neoplasm will be shown by an irregular diffusion of the contrast medium through the substance of the tumor, with varied density and unsharply defined margin. With cystic tumors of malignant type the outline will not be sharply defined and is irregular, whereas in a simple benign cyst there is a circular or oval opacity of uniform density, with sharply defined outline.—*Samuel G. Henderson, M.D.*

JONES, B. W., and HEADSTREAM, JAMES W. Vesicoureteral reflux in children. *J. Urol.*, Aug., 1958, *80*, 114–115. (From: The Department of Surgery, Division of Urology, University of Arkansas Medical Center, Little Rock, Ark.)

The authors report their experience with a study of 100 routinely admitted children who were subjected to voiding cystography. They presented no urologic complaints and the routine urine analysis was negative. They ranged in age from fourteen days to fourteen years, with an average of three and one-half years.

The examination consisted of the injection of 10 per cent sodium iodide through the urethral catheter by gravity until the flow stopped. Following this 1½ to 2 oz. more of the solution was added by using a bulb syringe, and an immediate roentgenogram was made. The catheter was removed and a voiding cystogram was then obtained with the patient in the supine position.

Of the 100 patients examined, only one exhibited vesicoureteral reflux. This patient was studied and found to have 180 cc. of residual urine, a bladder neck obstruction and moderate trabeculation of the bladder musculature. A transurethral resection of the bladder neck was performed.

This investigation supports the findings of those who claim that vesicoureteral reflux occurs only in the presence of demonstrable uropathy. The authors believe that the voiding cystogram is easier to obtain and generally more satisfactory than the delayed cystogram in children of this age group. They also believe that children with normal urinary tracts will not exhibit vesicoureteral reflux.—*George W. Chamberlin, M.D.*

CIBERT, J., and NAUDIN, E. P. L'examen radiologique dans les iléo-cystoplasties. (The radiologic examination in ileo-cystoplasties.) *J. de radiol., d'électrol. et de méd. nucléaire*, June–July, 1958, *39*, 358–367. (From: Clinique urologique de Lyon, Pavillon V, Lyon, France.)

A relatively recent conquest of urinary surgery is ileo-cystoplasty, by means of which the bladder is replaced or expanded with a loop of ileum. The latter is detached from the continuity of small bowel, its mesentery is preserved, and it is anastomosed to the bladder. It may either be left as a long segment, or joined to itself in the form of a ring.

Radiologists may properly evaluate patients by intravenous or retrograde urography for this procedure, which is useful in the small bladder of chronic cystitis (tuberculous or otherwise), after partial cystectomy for cancer, in paralysis of the bladder of neurologic origin, and in repair of the ureter. Postoperative studies have been done, and are extensively illustrated.

In a series of 78 cases there were 12 postoperative deaths, principally from paralytic ileus, emboli and pulmonary complications.—*Frank A. Riebel, M.D.*

AMAR, ARJAN D., and RATLIFF, RIGDON K. Gas gangrene of urinary bladder and abdominal wall following catheterization. *J. Urol.*, Aug., 1958, 80, 130–131. (From: The Department of Urology, St. Joseph Mercy Hospital, Ann Arbor, Mich.)

This is a case report of a seventy-six year old farmer with acute urinary retention who had previously been catheterized and on the day before admission had made an attempt at self-catheterization. Physical examination showed a rather debilitated white male with signs of avitaminosis, arteriosclerotic heart disease and congestive failure. The bladder was palpated above the symphysis pubis. The prostate gland was enlarged and benign in character. Catheterization of the bladder yielded 700 cc. of urine that looked like prune juice. The patient was put on dependent drainage and treatment for his congestive heart failure. On the second day of hospitalization, he complained of abdominal pain and the catheter stopped draining. The following morning he went into shock and the clinical diagnosis of ruptured bladder was made. On auscultation the abdomen was silent. A measured quantity of sterile water was recovered with slight deficit. A cystogram showed evidence of extravasation of contrast material outside the bladder, some of which extended along the lateral abdominal wall to the subcostal margin. This was noted to be an unusual distribution for intraperitoneal rupture of the bladder.

At operation there was evidence of foul smelling gas in the abdominal wall which had separated the transversalis fascia and produced a cavity which extended up to the costal margin and lumbar region on the right side. The peritoneum was found to be intact. Exploration of the gangrenous abdominal wall revealed a soft suprapubic area through which the exploring finger passed easily into the cavity of the bladder. Biopsy from this region showed evidence of gas gangrene and the culture was reported as *Clos-*

tridium perfringens with streptococci and *Escherichia coli.*

The abdominal wall was widely drained and washed with hydrogen peroxide and irrigated with oxygen through Dakin catheters. The patient was given the usual antibiotic and supportive therapy, but expired the following morning. No autopsy was obtained.

This case is important to the radiologist because of the unusual distribution of the opaque medium which was injected into the bladder and extravasated into the abdominal wall extraperitoneally. A possible mode of infection is discussed and the authors note that no other case of this nature has been found in the literature. One illustration is presented.—*George W. Chamberlin, M.D.*

David, Hugh J., and Telinde, Richard W. Urethral diverticula: An assay of 121 cases. *J. Urol.*, July, 1958, *80*, 34–39. (From: The Department of Gynecology, The Johns Hopkins Hospital, Baltimore 5, Md.)

Diverticula of the female urethra are more common than have been previously recorded. The most important single diagnostic item is a high index of suspicion. In 121 cases reviewed at the Johns Hopkins Hospital, only 71 were diagnosed prior to 1955, whereas 50 were found in a twelve month period of 1955 to 1956.

This study shows that there is no relation between the parity of the patient and the incidence of diverticula of the urethra. The average age was between twenty-five and forty-five years and no cases were diagnosed prior to the age of twenty. The symptoms were usually intermittent, the most important being frequency of urination, dysuria and urgency. Sixteen patients had a palpable mass from which pus could not be expressed and 12 patients showed a palpable mass from which pus was expressed. Unusual tenderness on digital examination of the urethra was present in 65 cases and 13 patients had tenderness over the lymphatics in the groin. Twenty-six patients had a negative urine analysis and 41 had pyuria and hematuria. Urinary culture showed most commonly the coli-aerogenes group.

In 1955 and 1956, 54 per cent of the group of patients were diagnosed by means of urethrography, whereas prior to 1955 none of the patients were diagnosed by this method. In the female, the urethrogram can be done by using the pressure technique with an inflated balloon in the bladder and one against the external urethral orifice. Diverticula with a small orifice which might be missed on direct endoscopic examination may be seen by this method.

The authors believe that every patient should have the benefit of urethrography prior to surgery. The existence of compound or multilocular diverticula cannot be predicted by cystoscopy or endoscopy alone. In some instances, multiple diverticula unseen by direct examination have been demonstrated by urethrography.—*George W. Chamberlin, M.D.*

Vanderhorst, L. F. Von P. Giant urethral calculus: A case report. *J. Urol.*, July, 1958, *80*, 31–33. (From: The Surgical Service, Winter Veterans Administration Hospital, Topeka, Kans.)

A calculus in the male urethra is not a rare occurrence. Usually these are small and may become lodged in a deep fold, or in a diverticulum.

A seventy year old patient who had preliminary symptoms twenty-two years before definitive surgery, was shown to have a calculus 3 by 5 cm. near the junction of the bulbous and membranous urethra. This patient had hematuria for one day twenty-two years prior to admission to the hospital. Following this he noted mild pain in the groin lasting one week. Some years later he gradually developed urinary frequency and nocturia at intervals of one to two hours. Intermittent hematuria was also present.

One week prior to hospitalization, the patient developed fever and chills. Physical examination showed that he was emaciated and acutely ill. A hard mass was palpable under the raphe of the perineum. The prostate was essentially normal to palpation. Roentgenographic examination of the pelvis revealed a radiopaque density of a somewhat laminated character below the symphysis pubis. The urethrogram demonstrated this calculus to be adjacent to the membranous urethra. Intravenous pyelography disclosed a poorly functioning left kidney with numerous calculi present. The right kidney and urinary tract were normal. An external urethrotomy was done and the stone was easily removed with forceps. An indwelling catheter was then passed and the urethra closed.

The author discusses the possibility of development of such calculus from a small stone which originally might have lodged in a urethral diverticulum in the region of Cowper's gland.—*George W. Chamberlin, M.D.*

Skeletal System

Lièvre, J.-A. (Paris, France.) Nouveau syndrome: ostéome endocranien, ostéomes du squelette, ostéomes des parties molles périphériques, histiocyto-fibrome cicatriciel. (A new syndrome: Endocranial osteoma, skeletal osteomas, osteomas in the peripheral soft tissues, cicatricial histiocytofibroma.) *Presse méd.*, June, 1958, *66*, 1143–1146.

A female, twenty-eight years of age, was seen April 1, 1955, because of bony masses in the soft tissues. In 1940, a tumefaction appeared slowly on the right instep. In 1942, a tumefaction was noted above the left patella. In 1943, a bony mass was removed

and osteotomy performed on the left instep. In 1947, surgery on the right wrist was necessary, and in 1950, an exostosis of the right instep and a tumefaction of the inferior portion of the anterior surface of the right thigh were present.

Roentgenographic study in 1950 revealed multiple lesions. In addition to the soft tissue masses, there was an opaque endocranial mass above the right petrous bone.

Laboratory data: blood calcium 97 mg.; alkaline phosphatase 2.2 Bodansky units; blood sugar 1.20 gm.

Microscopic examination of the exostoses removed in 1950 revealed bony tissue with the structure of spongiosa, very vascular trabecular spaces filled with fatty tissue and absence of myeloid elements. There was no evidence of suspicious activity.

Since 1950, bony tumors have re-appeared on the right instep and left internal malleolus. In March, 1955, physical examination was essentially negative aside from a number of pigmented nevi and the following lesions: On the external surface of the left arm was a firm, non-bony induration, 1 cm. in size, which appeared on a vaccination scar made in 1948; on the anterior surface of the right tibiotarsal articulation, there was a hard spherical mass which seemed to be adherent to the bone; both feet were held in equinus and there was practically no motion at the tibiotarsal articulation.

Roentgenographic study in March, 1955 demonstrated bone masses located in the following regions: (1) Situated in, but separated from, the superior border of the left petrous bone, about 18×20×10 mm. in size. There had been no change since 1950. (2) Extruding from D1-D4 on the right anterior side of the spine in the gutter and about 15 mm. wide. (3) Extending from L1-L3, separated about 40 mm. from the spine and partly subcutaneous in the lumbar gutter, 65 mm. long and 10 mm. wide. (4) In the soft tissues of the right forearm. (5) In the soft tissues about the left hip; an elongated density in the neck of the left femur. (6) An enlarging bone mass in the right thigh separated from but parallel to the femur; on the left side, a similar mass at the inferior border of the patella. (7) At the left ankle.

The microscopic examination of the scar at the vaccination site revealed histiocytofibroma. The bone masses were composed of adult bone with no evidence of activity. Most of these bone lesions were clearly separated from the normal skeleton, but the one at the right astragalus was in continuity with the bone and had to be separated by bone scissors.

This new syndrome is characterized by soft tissue osteomas, skeletal osteomas and endocranial osteoma (or opacity). The patient was a large girl with a masculine build but no signs of acromegaly or gigantism. The syndrome is thought to be of genetic origin. There may be a relation to Gardner's syndrome (colonic polyposis, multiple osteomas, soft tissue tumors) presenting in a different form.—*Marcy L. Sussman, M.D.*

JACKSON, ASHLEY. Thinning of the parietal bones. *Proc. Coll. Radiologists, Australasia*, Dec., 1957, *1*, 74–76. (From: The School of Radiology, R. P. A. Hospital, Sydney, N.S.W., Australia.)

Parietal thinning is probably of no clinical importance except to differentiate it from pathologic conditions in the calvarium. It is the result of dysplasia or atrophy of the diploe in both, or less commonly in one, of the parietal bones. It produces flattening or longitudinal grooving of the bones in their central portions involving about 25 per cent of the parietal area. The periosteum remains intact on both sides.

The exact etiology is obscure, but Steinbach and Obata point out that this is the only area of the skull that is not the site of muscle attachments and explain the thinning as a result of decreased osteoblastic activity associated with gonadal insufficiency, senility or other causes of osteoporosis.

Roentgenologic features include two recognized types of thinning: (1) Flattened or depressed, triangular or quadrilateral areas in the parietal bones and (2) longitudinal grooving along either side of the sagittal suture. This is best seen in the posteroanterior projection as is the characteristic crest-like ridge of intervening bone which separates the parietal depressions. The lateral view shows an area of decreased density in the parasagittal region with a smooth regular, well defined lower border parallel to the skull base. Incidental osteoporosis of the spine was observed by Epstein in 30 per cent of his series.

Because of the usual symmetric appearance of this thinning, it is readily diagnosed but should not be confused with enlarged parietal foramina, epidermoids, osteoporosis circumscripta, metastatic lesions or xanthomatous defects.

Two cases are presented, both in elderly white females in whom the condition was discovered incidentally.—*Louis C. Lippert, M.D.*

ELLIS, MAURICE. Fractures of the parietal bone in children. *Lancet*, May 17, 1958, *1*, 1048–1051. (From: Casualty Department, General Infirmary, Leeds, England.)

The author believes that there is a type of fracture of the parietal bone in children which has distinct clinical features. He describes the findings in 12 cases observed between 1955–1957.

The typical clinical picture is that of a small child with a characteristic lump on the side of his head. The lump is soft and cystic and usually 3 to 4 inches in diameter. It is circular in outline and there is no bruising of the overlying skin. The roentgenogram shows a fracture of the underlying parietal bone. The

lump disappears in twelve to twenty-one days after its appearance and the child remains well during the entire process.

It is postulated that the lump is produced by spinal fluid which seeps through the fracture and collects between the galea aponeurotica and the periosteum of the skull. Aspiration of the lump in one case seemed to substantiate this theory.—*Richard E. Kinzer, M.D.*

Currarino, Guido, and Silverman, Frederic N. Premature obliteration of the sternal sutures and pigeon-breast deformity. *Radiology*, April, 1958, *70*, 532–540. (Address: G. Currarino, The Children's Hospital, Cincinnati, Ohio.)

The authors present 3 cases of an uncommon developmental anomaly of the sternum characterized by premature obliteration of the sutures, a tendency toward forward angulation, and a corresponding increase in the sagittal diameter of the thorax. An excellent review of the literature concerning the embryologic development of the sternum is given.

The 3 patients presented in this paper showed a solidly synostosed sternum at an abnormally early age. In addition, the sternum of each of the 3 infants exhibited a forward angulation in the middle third or proximal half. At the site of the angulation, there was midline protrusion of the anterior chest wall with a localized increase in the sagittal diameter of the thorax resembling the arcuate type of pigeon breast deformity described by Lester. This anomaly is considered by the authors to be the result of inadequate segmentation of the sternum during fetal development and consequently of poorly formed suture lines which lead to premature ossification.—*John S. Alexander, M.D.*

Leonard, Morton H., Hart, Maynard S., and Eckfeldt, Roger W., Jr. Nonossifying fibroma of bone; successive lesions in the same tibial metaphysis. *Radiology*, April, 1958, *70*, 582–584. (Address: M. H. Leonard, Hotel Dieu Sisters' Hospital, El Paso, Texas.)

The authors present a case of nonossifying fibroma of bone which recurred in the tibial metaphysis of a seven year old child. In the opinion of the authors, the occurrence of 2 distinct successive lesions of nonossifying fibroma of bone in the same tibial metaphysis may be explained on the basis of a growth disturbance rather than a true neoplasm.

The child was first seen on Feb. 1, 1954, following an injury. Roentgenograms revealed an infraction of the lateral tibial cortex through an oval, loculated area of radiotranslucency. There were no other skeletal lesions. An excisional biopsy of this area was done along with bone grafts. The pathologic report of the biopsy was that of nonossifying fibroma of bone. The patient did well postoperatively and a subsequent roentgenogram revealed filling-in of the radiotranslucent area. Fourteen months later, roentgenograms showed complete healing of the operated area but a new zone of rarefaction, distal and distinct from the original, was discovered. This new site increased in size and twenty-eight months postoperatively, the child again underwent surgery. Biopsy revealed tissue identical with that of the first specimen.—*John S. Alexander, M.D.*

Williams, Rohan E. Multiple myeloma. *J. Fac. Radiologists*, Jan., 1958, *9*, 2–12. (From: Radiological Department, St. Mary's Hospital, London, W.2, England.)

Clinically, multiple myeloma is dominantly a disease of the 5th, 6th and 7th decades of life, and it is twice as common in men as in women. The outstanding clinical features are pain, tumor formation, deformity and pathologic fracture. Pain is present in up to 90 per cent or more of reported cases, varying from mild soreness to excruciating pain. Pathologic fracture occurs most often in the vertebral column and ribs. Palpable tumor is found commonly in the ribs, sternum and skull. It may vary in size from time to time, even without treatment. Deformity following pathologic fracture may involve the vertebral column, especially the thoracic spine, sternum, ribs or long bones. Mucopurulent bronchitis and recurrent attacks of pneumonia, particularly in patients with high serum protein, may be seen frequently in multiple myeloma.

From a neurologic standpoint signs and symptoms may be due to (1) mechanical compression of cord or nerve roots from vertebral collapse, (2) myeloma tissue extending outward from adjacent bones, and (3) peripheral neuritis without demonstrable nerve involvement.

Severe renal functional impairment, particularly in patients with Bence Jones proteinuria, is seen in a high proportion of cases. Blood urea is often high, but hypertension is rare, and the author believes that normal or low blood pressure with nonprotein nitrogen retention is highly suggestive of myelomatosis.

Bone involvement may be seen initially with single or several widely scattered osteolytic foci, and sternal puncture may be negative at this time. After months or years generalized multiple myelomatosis will usually ensue.

In multiple myeloma there are three abnormalities of protein metabolism which are not found in any other neoplastic lesion affecting the skeleton: Bence Jones proteinuria, hyperglobulinemia and primary amyloidosis or paramyeloidosis. The occurrence of Bence Jones proteins is almost pathognomonic of multiple myeloma. There appears to be an inverse relationship between Bence Jones proteinuria

and hyperglobulinetmia—proeinuria being more common when serum globulin values are low. The total serum proteins will be elevated in the majority of cases of multiple myeloma. However, the serum albumin at times may be markedly reduced, so that even with elevation of globulins the total protein may not be high. One may get marked inversion of the normal albumin globulin ratio of 1.2:1, and this may reach 1:10. In some cases of multiple myeloma the mesodermal tissues, particularly those of the heart, the blood vessels and the intestines, may contain amyloid deposits.

The roentgenographic features of multiple myeloma can be grouped in three main categories: (1) Multiple rounded zones of complete bone destruction, with sharp or moderately clear cut margins; (2) single zonal areas of bone destruction, tending to be larger than in the multiple rounded lesions; and (3) a widespread patternless osteoporosis, especially in the spine, or a diffuse granular osteoporosis. In none of these manifestations does one see new bone formation, except after irradiation, or as callus formation after a pathologic fracture. Such fractures are common, and are found in over 60 per cent of all cases—particularly in the vertebrae, ribs, femora and humeri. The author states that an almost pathognomonic finding is that of chest roentgenograms showing multiple ill-defined soft tissue opacities with curvilinear margins encroaching on the lung fields. Coincident with each of these, a zone of rib destruction, with or without a pathologic fracture, will be found. When a long bone is involved, multiple foci tend to be grouped together in one part of the bone, with little or no change in the remainder of the bone. The author further states that myelomatosis can be very extensive as shown at autopsy, with very little obvious osseous change on roentgenograms. It follows that when roentgenographic changes are present the myelomatous involvement is almost always much greater than appears on the films.

Radiation therapy has a very useful role in the management of this disease. One case report is given. This patient survived sixteen years after the histologic diagnosis, many of the myelomatous deposits being highly radiosensitive.—*Samuel G. Henderson, M.D.*

VIERNSTEIN, K., and HIPP, E. Wirbelsäulen-Ganzaufnahmen mit der Verlaufsfolie. (Roentgenograms of the entire spine with the gradient screen.) *Röntgen Blätter*, March, 1958, *11*, 79–81. (From: Orthopädische Klinik und Orthopädische Poliklinik der Universität, München, Germany.)

In the past few years four methods have been introduced for the production of a single roentgenogram of the entire spine: (1) Application of lead plates on and beside the patient's spine to reduce stray radiation and to diminish the effective beam in selected areas of the spine; (2) use of a rotating compensating diaphragm between the tube aperture and the patient; (3) use of a swinging compensating diaphragm between the tube aperture and the patient; and (4) employment of a compensating supplementary filter composed of copper and aluminum sheets.

A simpler method for overcoming the differences in radiability of the various portions of the spine is presented by the authors in the form of intensifying screens with gradually decreasing intensifying capability from end to end. The intensifying screens consist of special calcium-tungsten composition sheets corresponding in thickness to various thicknesses of the spine. The span of fluorescent intensity between the weak and strong ends of the calcium-tungsten screen is about 1:4. This varying fluorescent intensity of the screen compensates for the contrast differences due to differences in absorption when roentgenography of the entire spine is attempted.

The authors believe that the use of their special gradient screen allows simple and efficient roentgenography of the entire spinal column. One illustration supports their contention.—*Harold E. Fulton, M.D.*

HUBBLE, DOUGLAS. (Derby, England.) Discussion on skeletal manifestations of general disease. *Proc. Roy. Soc. Med.*, July, 1958, *51*, 475–479.

This is a brief summary of the clinical aspects of osteoporosis, hyperparathyroidism, primary and secondary, and the osteoporosis associated with corticosteroid therapy. Several cases are reported, one with a chronic renal lesion and phosphorus retention followed by osteitis fibrosa and parathyroid hyperplasia. Functioning parathyroid adenoma developed so that the patient had secondary hyperparathyroidism and then primary hyperparathyroidism. —*Martha Mottram, M.D.*

STEINER, R. E. (London, England.) Discussion on skeletal manifestations of general disease. *Proc. Roy. Soc. Med.*, July, 1958, *51*, 479–485.

In osteoporosis there is a diffuse decrease in density with a thin cortex and trabeculae; vertebral fractures are common; Looser zones never occur; the interveterbral disks are widened. In osteomalacia there is a general decrease in bone density often with considerable deformity, fish-tailed vertebrae, pseudofractures. In primary hyperparathyroidism there are varied manifestations. Frequently the skeletal structures are normal; there may be renal calculi only; or there may be bone cysts, generalized decreased bone density with deformity of the skeleton and pathologic fractures, and subperiosteal cortical erosions in the phalanges and along the cortex of the long bones near the joints. Secondary hyperparathyroidism occurs in chronic uremia, tubular kidney defects and late in osteomalacia. The roentgen

changes are those of primary hyperparathyroidism but bone cysts are rare. Some of the causes of increased and decreased bone density are listed.

The author notes that the interpretation of bone density depends largely on the observer's experience and the patient's age, sex and body build. For a routine survey he takes an anteroposterior roentgenogram of the hands and feet with a standard, a roentgenogram of one long bone, an anteroposterior roentgenogram of the pelvis, a lateral roentgenogram of the thoracolumbar spine and a lateral roentgenogram of the skull.—*Martha Mottram, M.D.*

Sissons, H. A. (London, England.) Histological changes encountered in some generalized skeletal diseases. *Proc. Roy. Soc. Med.*, July, 1958, *51*, 485–489.

In osteoporosis there is a reduction in the amount of bone tissue without a defect in its mineralization. The absence of quantitative information on the normal range of skeletal structures makes the histologic recognition of minor degrees of osteoporosis uncertain.

In osteomalacia there is an excess of osteoid tissue due to failure of calcification. Its recognition depends on use of one of two technical histologic procedures or microradiography.

Diffuse osteitis fibrosa (as distinguished from fibrous dysplasia where there are multiple circumscribed lesions) is associated with primary or secondary hyperparathyroidism. "Brown tumors" and cysts may appear in the primary condition, while in the secondary form there is excess osteoid tissue and abnormal structural architecture of bone. There is a wide range of bone changes in these conditions.—*Martha Mottram, M.D.*

Blood and Lymph System

Shafer, William A., and Lechner, Carl B. Cerebral angiography with miokon. *Radiology*, April, 1958, *70*, 557–560. (Address: W. A. Shafer, 609 Sassafras St., Erie, Pa.)

The authors discuss their experience with a series of 50 patients in whom cerebral angiography was done with the use of miokon sodium 30 per cent. None of the patients developed any untoward reactions or serious complications. Routine sensitivity tests were performed on all the patients. Contraindications for its use are the same as for any other iodine-containing contrast material.

The quality of the roentgenograms has been excellent and good visualization of the vessels has been consistently obtained. As there is no irritation of the vessels, the patient does not move during the injection of the medium and exposure of the films. This permits relatively longer exposure times during which more vessels are outlined by the medium during the arterial phase. No striking change in the visualization of the venous or capillary phases has been evident. The technique used by the authors for this procedure is described.—*Donald N. Dysart, M.D.*

Husebye, Kjeld O., Wolff, Herman J., and Freidman, Louis L. Aortic dissection in pregnancy: A case of Marfan's syndrome. *Am. Heart J.*, May, 1958, *55*, 662–676. (From: The Charles T. Miller Hospital, St. Paul, Minn.)

The authors discuss aortic dissection in pregnancy with particular reference to a patient with Marfan's syndrome, in whom the original dissection occurred during the twenty-second week of the pregnancy. They carried the patient to a successful conclusion of her pregnancy, using cesarean section two weeks ahead of term, instead of following the usual method of treatment of cardiacs. Thirteen months after the initial dissection, the patient died suddenly of congestive failure as identified at autopsy. A smaller than normal amount of elastic tissue bulk was noted in the aorta.

In a study of 105 cases of Marfan's syndrome, no ill effects of pregnancy were note. In 51 cases of aortic dissection during pregnancy, one being the present case, 3 were known to have Marfan's syndrome.

The authors suggest that the incidence of 3 cases of Marfan's syndrome in 51 cases of aortic dissection during pregnancy is too high to attribute to chance, and that Marfan's syndrome as the cause of aortic dissection in pregnancy is probably overlooked in many instances. They raise the question whether an absolute decrease in elastic tissue bulk is a constant feature in Marfan's syndrome.

They believe that pregnancy enhanced the aortic dissection in their patient and shortened her life. They recommend interruption of pregnancy (if dissection occurs early) and cesarean section if it occurs during the third trimester and the fetus is viable.—*P. B. Parsons, M.D.*

Eastcott, H. H. G., and Sutton, David. Chronic dissecting aneurysm of the aorta diagnosed by aortography. *Lancet*, July 12, 1958, *2*, 73–75. (From: St. Mary's Hospital, London, W.2, England.)

Recorded cases of chronic dissecting aneurysm diagnosed during life are few. Even less common is positive proof of the diagnosis before necropsy. The patient whose case is reported here was suspected of having an aneurysm of the abdominal aorta, but an unsuspected dissecting aneurysm was demonstrated by translumbar aortography. The original lumen of the aorta was later clearly visualized by a subsequent aortogram through percutaneous femoral catheterization. The aneurysmal sac began near the aortic arch and terminated in the common iliac arteries.

Dissecting aneurysms of the aorta are usually

fatal, but a few patients occasionally survive the initial episode and may live for many years with the condition unrecognized. Such nonfatal aneurysms are often of the "double-barrelled aortas" (Drury) extending at or near the aortic arch to the bifurcation. The patent lumen may become lined with endothelium and may contain varying degrees of atheromatous changes. The length of the aneurysm readily equalizes the pressure at the point of primary tear and prevents rupture. A re-entrant tear may develop in the distal aorta due to reduced pressure by successive branching. Local factors in the structure of the distal aorta and the iliac arteries may also be important.—*J. T. Ling, M.D.*

ELLZEY, ROBERT F. A serial and chronographic method of aortography and bilateral arteriography of the lower extremities. *Radiology*, April, 1958, *70*, 551–556. (Address: 1050 Clermont St., Denver, Colo.)

Ideally, arteriography should show the entire vascular ramifications from the point of exploration to the end of the limb; it should be serial to show the characteristic moments of the filling of the network into which the injection was made by a series of roentgenograms taken at intervals of seconds; and it should be chronographic, with measurement of the time intervals between the beginning of the injection of the opaque medium and the various roentgenographic exposures. This is done by using a movable roentgenographic table with a Sanchez-Perez seriograph centered beneath the table at the abdominal aorta and the tube centered to the changer. An abdominal aortic puncture is performed in the conventional manner, usually above the renal arteries at the level of D-11. Usually 25 to 30 cc. of contrast medium is used. Just before the last 5 cc. of the medium is injected, the first exposure is made and the table is advanced cephalad a distance of 10 inches according to predetermined marks on the floor relative to the rear wheel axle to be in position for the second exposure. The seriograph is set for intermittent exposures and is controlled by the radiologist. The procedure is continued until the ankles have been exposed and can then be reversed, with serial exposures from the ankles to the pelvis again. The exposure time is altered between serial exposures to compensate for variations in extremity thickness. The rate at which the table is moved must be varied because of the rapid filling of the iliac and femoral arteries and the more delayed filling of the popliteal and tibial arteries. A timer is attached to the seriograph so that the exact time of exposure is recorded on each film.—*Walter H. Jarvis, Jr., M.D.*

FINEBERG, CHARLES, SCHECHTER, DAVID C., and BARRICK, CLAUDE W. Gangrene of the large intestine and ovaries after translumbar aortography; report of a case. *J.A.M.A.*, July 5, 1958, *167*, 1232–1236. (Address: C. Fineberg, 1025 Walnut St., Philadelphia, Pa.)

Translumbar aortography is frequently used as a valuable diagnostic adjunct in the investigation of the retroperitoneal structures and blood vessels. The injury attendant on translumbar aortography is small; the complications subsequent to the procedure are serious when they do occur. One of the rarest complications is mesenteric artery thrombosis.

The authors report a case of gangrene of large intestine and ovaries following translumbar aortography with survival of the patient after surgical intervention. In their case the major portion of the contrast medium was injected into a false channel outside of the true lumen of the aorta. This had been probably initiated when the tip of the needle entering the sclerotic wall of the aorta had elevated an atheromatous plaque thus creating a new plane along which the contrast medium had dissected.

Mesenteric artery thrombosis occurs if one or a combination of the following factors is present: (1) too great an injection pressure; (2) too large a volume of contrast material; and (3) the use of too toxic and irritating contrast medium.

Most of the fatalities from translumbar aortography resulted when inorganic iodides were used. The organic iodine compounds are admittedly less dangerous. However, renal and spinal cord damage has been reported irrespective of the type of contrast medium employed. Not more than 25 ml. of contrast medium should be used per study and repeated injections should be avoided. A diluted test dose is advocated to determine the location of the needle.—*Ahmad Hatam, M.D.*

FADEM, CHARLES, and LYONS, HAROLD A. Concentrated hypaque sodium for angiocardiography; preliminary report. *Radiology*, May, 1958, *70*, 732–735. (Address: C. Fadem, 451 Clarkson Ave., Brooklyn 3, N. Y.)

The authors report their results using a new angiocardiographic medium, hypaque-M, 90 per cent. The study consisted of 38 injections in 23 patients, 15 of whom had 2 consecutive injections for the purpose of obtaining roentgenograms in additional views. A 12-gauge needle was inserted intravenously and a sensitivity test dose of 2 cc. was injected first. Following this, 45 to 50 cc. of the hypaque solution was rapidly injected within less than two seconds. After the roentgen examination, 100 cc. of saline solution was rapidly injected to "wash out" the hypaque to prevent a chemical phlebitis.

No severe reactions were encountered and such subjective symptoms as flushing, and nausea and vomiting were few and mild in degree. The urticaria that was noted in 3 cases was limited in area and disappeared in approximately one hour. There were no incidences of postinjection phlebitis.

The authors believe that 90 per cent hypaque is superior to 70 per cent urokon for roentgenographic visualization of the thoracic cardiac and vascular structures. Changing contrast media to avoid sensitivity reactions when repeat angiocardiograms are to be done at a later date is suggested. Thus, urokon and hypaque may be used alternately for this purpose.—*John S. Alexander, M.D.*

Kaindl, F., Mannheimer, E., and Thurnher, B. Lymphangiographie und Lymphadenographie am Menschen. (Lymphangiography and lymphadenography in humans.) *Fortschr. a. d. Geb. d. Röntgenstrahlen u. d. Nuklearmedizin*, July, 1958, *89*, 1–13. (From: II. Medizinische Universitätsklinik, Wien, Austria.)

The authors relate their experiences with the roentgen examination of the lymph channels and nodes in 140 patients.

According to Kinmonth, the lymph vessel changes may be classified as follows: (1) Primary lymph vessel changes: (a) hypoplasia, where the vessels are thin and few in number; (b) lymphectasia, divided into lymphedema congenital praecox (in those under the age of 35 years), and congenital tardum (in those past the age of 35 years). (2) Secondary lymph vessel changes: Post-phlebothrombosis syndrome, post-traumatic changes, and residua after inflammatory changes in pelvic structures (adnexitis, incomplete abortion).

Lymphadenography gave the following results: In lymphatic leukemia, the lymph nodes are always enlarged and sharply outlined. The inner structure of the node shows a very fine "ball of thread" configuration. The appearance in Hodgkin's disease is that of dilated afferent lymphatic channels, with the nodes showing no details of their inner structure. In lymphosarcoma, melanosarcoma, and carcinoma there is a cup-like indentation where the lymph vessel enters the node. The nodes themselves are seen only as a shell, with the roentgen-opaque material visualized along the periphery of the node.—*Samuel Richman, M.D.*

RADIATION THERAPY

Sinclair, W. K., Laughlin, J. S., Rossi, H. H., Ter-Pogossian, M., and Moss, W. S. Intercomparison of x-ray exposure dose using Victoreen dose meters at various energies, particularly 22 Mevp. *Radiology*, May, 1958, *70*, 736–745. (Address: W. K. Sinclair, Physics Department, M. D. Anderson Hospital, Houston 25, Texas.)

The authors report intercomparisons of the roentgen exposure dose measurement procedures employed in 5 institutions which use or have recently used 22 mev. peak roentgen rays for clinical and biologic purposes. The institutions concerned were: Memorial Hospital (New York), Presbyterian Hospital (New York), M. D. Anderson Hospital (Houston), Mallinckrodt Institute of Radiology (St. Louis) and the University of Illinois (Chicago). The determination of exposure dose in each institution is based on a different calibration procedure, although each employs a Victoreen instrument. The calibration procedures were compared by first examining the factors associated with the methods of exposure and then using a satisfactory exposure procedure, making simultaneous comparisons.

The results show that the various types of lucite calibration blocks in use have little influence on the measurements. Differences arise, however, from the application of different correction factors. At the M. D. Anderson Hospital the correction factor for cobalt 60 radiation is applied to its Victoreen chamber, while the Memorial and Presbyterian Hospitals use Victoreen correction factors for 200 kv. radiation. This results in a difference of about 8 per cent, the nominal roentgen at M. D. Anderson Hospital at this energy being smaller than the others. This is not a difference of measurement. The difference is due to the corrections believed to be necessary to the measurement after it has been made. The intercomparison was undertaken in order to establish the relationship of these estimates to one another.—*A. W. Sommer, M.D.*

Andriska, Jolán, Frigyesi, Gyula, Kiszely, György, and Nagy, Mária. Die Wirkung einer grossen Dosis Röntgenstrahlen auf die Entwicklung eines menschlichen Foetus. (The effect of a large dose of roentgen rays on the development of a human fetus.) *Strahlentherapie*, April, 1958, *105*, 630–638. (From: Röntgenabteilung des Krankenhauses des Gemeinderates von Székesfehérvár and Histologisch-embryologisches Institut der Medizinischen Universität in Budapest, Budapest, Hungary.)

From February 11 to 25, 1955, a twenty-one year old woman received 1,800 r (no further physical factors cited) both anteriorly and posteriorly to her pelvis in the treatment of a metastasis in her left sacral wing. On a roentgenogram taken March 1, 1955, a fetal skeleton, estimated to be at three months' gestation, was demonstrated. At the fifth to sixth month of gestation, on June 12, 1955, the fetus, uterus and the adnexal structures were excised.

Gross examination of the fetus showed no abnormality. Dissection of the fetus and histologic examination of its tissues showed changes of the central nervous system, broadly summarized as delayed development (agenesis of the corpus callosum, underdevelopment in the corpus striatum, alterations in the nerve and glial cells). Evidence of repair was

present and the stratification of the cerebral cortex appeared normal. The changes in other organs were not serious enough to alter development of the fetus in a major fashion (retardation of development of the renal glomerular system, vacuolization of pulmonary alveolar epithelium, bullous changes or desquamation of intestinal epithelium, etc.).

The maternal ovaries showed extensive stromal fibrosis, a few scattered primordial follicles, and only traces of a Graafian follicle.—*Henry G. Moehring, M.D.*

DESBAILLETS, P. Le traitement hormonal des métastases généralisées du cancer du sein. (Hormonal treatment of generalized metastases in cancer of the breast.) *Schweiz. med. Wchnschr.*, Aug. 9, 1958, *88*, 777–782. (From: Clinique médicale universitaire, Lausanne, Switzerland.)

The evolution of generalized carcinoma of the breast can be modified by endocrine therapy. With patients who still menstruate or who have stopped in the preceding year or two, castration should be considered first, as at that stage of life breast metastases are easily stimulated by estrogens. Castration may be performed either radiologically or surgically, and will benefit one-third of the patients subjectively or objectively. While radiation treatment is more easily applied, surgery is preferred when the case is evolving rapidly.

Androgens may be prescribed at any age, for with young women their action is anti-estrogenic, and with older women they supposedly stimulate the defensive processes against cancer. Their most striking effect is on bone metastases, where they usually relieve pain rapidly and sometimes produce objective regression. They may, however, produce a hypercalcemia.

Estrogens must be kept for the treatment of carcinomas which are independent of ovarian function, as in aged women. They give striking results, chiefly on metastases of soft tissues and particularly of the skin. Unfortunately they will aggravate any heart failure which is already present.

Cortisone and ACTH are seldom advisable.

Adrenalectomy serves to eliminate a secondary source of estrogens, and can be applied in cases which have been temporarily benefited from castration, but in which recurrence has developed. The same applies to hypophysectomy, which some authors consider easier to perform.

Hormonol therapy does not exclude radiation therapy, which is useful for its local beneficial effects.—*Frank A. Riebel, M.D.*

RADIOISOTOPES

WERNER, SIDNEY C. The effect of triiodothyronine administration on the elevated protein-bound iodine level in human pregnancy. *Am. J. Obst. & Gynec.*, June, 1958, *75*, 1193–1196. (From: The Departments of Medicine and of Obstetrics and Gynecology, College of Physicians and Surgeons, Columbia University, and the Presbyterian Hospital, New York, N. Y.)

Fifty-six normal patients in the second and third trimester of pregnancy were studied regarding the effect of the administration of 75 to 125 μg. of triiodothyronine for eight days on the protein-bound iodine level in the blood. Two cases ending their third month of pregnancy were also studied regarding the I^{131} uptake following eight days of triiodothyronine administration.

This study again confirms that there is a physiologic increase in pregnancy in the protein-bound iodine level and also that the administration of triiodothyronine produces a definite depression in the protein-bound iodine level. Larger doses of triiodothyronine were needed to depress the protein-bound iodine levels in the last trimester. This was thought to be due to an increased demand for the thyroid hormone in the third trimester of pregnancy.

It is believed that the elevated protein-bound iodine level in pregnancy is due to an increase in binding capacity of the specific carrier protein of the serum for thyroxine.

The I^{131} uptake was also depressed by the administration of triiodothyronine.

The data obtained from this study suggest that a normally responsive pituitary-thyroid relation is present in pregnancy and that there is very little, if any, thyrotropin excretion by the placenta.—*Charles W. Cooley, M.D.*

FOUNTAIN, JAMES R. Haemorrhagic thrombocythaemia; report of two cases treated with radioactive phosphorus. *Brit. M. J.*, July 19, 1958, *2*, 126–130. (From: Department of Medicine, the General Infirmary, Leeds, England.)

The term hemorrhagic thrombocythemia was first suggested in 1934 by Epstein and Goedel for the bleeding disorder which is characterized by a persistently raised platelet count. This disorder is very rare and probably less than 30 cases have been reported in the world literature.

Hemorrhagic thrombocythemia is usually associated with other myelo-proliferative disorders or splenic atrophy. It may follow splenectomy but is rarely primary in that it is unassociated with other pathologic processes. The mechanism of the bleeding tendency is unknown. Half of the reported cases showed abnormal bleeding times, but the other routine hemostatic function tests were usually normal.

Two cases were presented and the clinical and

hematologic features were described in detail. Mortensen in 1948 regarded thrombocythemia as allied to polycythemia and leukemia and observed some beneficial effects from total body irradiation. In view of these findings, the 2 cases were treated with P^{32}. The response was very satisfactory and bleeding ceased as the platelet count returned to normal. Further injections of P^{32} were given when the platelet count rose above normal and the patients have remained free from the bleeding episodes for eight and nine months. The leukocyte count returned to normal in the first case; in the second case when the hemorrhagic tendency was controlled the erythrocyte count rose to a polycythemic level. P^{32} was given in doses of 3 mc; the first case had a total of 9 mc of P^{32} and the second case 6 mc of P^{32}.—*Charles W. Cooley, M.D.*

Lawrence, John H., and Donald, William G., Jr. Giant follicular lymphoblastoma: Its treatment with radioisotopes. *Ann. Int. Med.*, July, 1958, *49*, 1–16. (From: The Donner Laboratory and Donner Pavilion, University of California, Berkeley, Calif.)

Giant follicular lymphoblastoma was described by Brill and associates in 1925 and by Symmers in 1927. It was originally thought to be a benign condition, but it was soon recognized that it was or could transform into a malignant disease of the lymphosarcoma type. The disease is very sensitive to irradiation and roentgen therapy to tumor masses has been the preferred treatment particularly when the disease is relatively well localized. Radioisotopes have been of value in widespread involvement.

Twenty cases with biopsy diagnosis of giant follicular lymphoblastoma that were seen between 1940 and 1955 are presented in this paper. Sixteen cases were followed to their termination; 2 are still living and 2 were lost to follow-up. Fourteen cases had received previous roentgen therapy. Three cases were in the terminal stage when first seen. Sixteen cases received P^{32} therapy. Fairly small doses of P^{32} were given intravenously at variable intervals to place the disease constantly under control. Complete blood cell counts were made repeatedly to determine the degree of bone marrow suppression and the duration of therapy was determined accordingly. The usual fractional dosage employed was approximately 1 mc and the usual interval was one week. The dosage was individualized, however. A single dose as high as 5.1 mc was given and intervals up to two months have been used.

Eleven patients received adequate P^{32} therapy. Three patients showed excellent response, with one exhibiting complete, and two nearly complete remissions. Three patients had good response with duration of control from seven to twenty months. Three patients had fair response, but required additional local roentgen therapy for control. The 10 cases which were adequately treated with P^{32} and followed to termination showed an average duration of the disease of 6.7 years as compared to the average in the literature of 6.0 years.

Radioactive phosphorus with local roentgen therapy or alone may be the treatment of choice in giant follicular lymphoblastoma and especially in cases of generalized involvement.—*Charles W. Cooley, M.D.*

Elkins, H. B., Flocks, Rubin H., and Culp, David A. Evaluation of the use of colloidal radioactive gold in the treatment of prostatic carcinoma. *Radiology*, March, 1958, *70*, 386–389. (From: University Hospital, Iowa City, Iowa.)

The authors present an analysis of cases of prostatic carcinoma treated with radioactive colloidal gold at the University of Iowa Hospitals during the past six and one-half years. In all, 552 patients received radiogold treatment. One hundred and thirty-five of these patients were treated over five years ago. Originally only those patients having biopsy-proved carcinoma of the prostate extending clinically beyond the confines of the capsule but limited to the local area were considered suitable for treatment by radioactive gold. Some of these patients had extensive local disease, which is now regarded as a contraindication for the use of radioactive gold. At present, more radical surgical procedures are used for removal of involved lymphatics, while control of the primary lesion is still attempted by irradiation.

The simple procedure of direct injection with a shielded syringe was found to be the quickest and safest as well as the easiest method. Speed and distance and a well-trained operating team are more effective than complicated apparatus. The final results are apparently independent of dose between the range of 0.5 and 2.5 mc per estimated gram of prostatic tissue. The actual volume of injected material is of considerable importance. Overdistention of the seminal vesicles may lead to rupture of the genital fascial envelope. As a result of poor technique as much as 80 per cent of the injected material may enter the blood stream.

A retropubic approach, with injection of radioactive material under direct vision, was used in about 70 per cent of the cases. Complications such as rectal ulceration, leukopenia and calculus formation occurred in about one-fourth of the first 50 treated cases. Subsequently the total percentage of complications dropped to 6.5.

Forty-six patients (34 per cent) survived five years or more. Thirty-two are alive without clinical evidence of disease. This leads to the conclusion that the method shows sufficient promise to justify continued study.—*Arno W. Sommer, M.D.*

ALLEN, WILLARD M., SHERMAN, ALFRED I., and CAMEL, H. MARVIN. Radiogold in the treatment of cancer of the cervix. *Radiology*, April, 1958, *70*, 523–527. (Address: W. M. Allen, School of Medicine, Washington University, St. Louis 10, Mo.)

The authors report the results of clinical studies with radiogold in the treatment of cancer of the cervix. The treatment of Stage I and Stage II cases has been fairly well standardized. The primary lesion is first treated with radium in doses ranging from 4,000 to 5,500 milligram hours. About two weeks after the radium application, 50 to 70 millicuries of radiogold are injected into each parametrium. The total dose is diluted to 70 cc. with saline solution. About two weeks after the injection of gold a decision is reached whether or not Wertheim hysterectomy and pelvic lymphadenectomy are to be done. If the patient is a good surgical risk the operation is performed about four weeks after the gold injection. The treatment of Stage III lesions is essentially the same except that the Wertheim operation is not done and the total amount of irradiation is raised to the maximum.

During the first seven years (1950–1956), 291 patients were treated with radiogold. In this series there were 3 ureterovaginal fistulas, 2 vesicovaginal fistulas, and 7 cases of ureteral obstruction. Neuritic pain, due to irradiation of the obturator nerves and the nerves forming the sacral plexus, was a frequent complication, usually persisting for 2 or 3 weeks. The over-all three-to seven-year salvage rate in 175 cases treated with radiogold is appreciably better than the five-year salvage rate in patients treated with roentgen therapy and radium. The salvage rate in the gold series is 85.3 per cent in Stage I, 69.4 per cent in Stage II, and 52 per cent in Stage III.

The following advantages are claimed for this method: (1) the cost is no greater than with roentgen therapy or with other forms of external irradiation; (2) the reaction in the patient is minimal; (3) the injection technique is relatively simple.—*Arno W. Sommer, M.D.*

RUF, HUGO, and HELLRIEGEL, WERNER. Zur Behandlung von Hirntumoren und metastasierenden Geschwülsten durch radioaktives Gold. (Radioactive gold in the treatment of cerebral tumors and metastasizing growths.) *Strahlentherapie*, May, 1958, *106*, 123–126. (From: Neurochirurgische Abt. der Nervenklinik der Stadt und Universität Frankfurt a. M. and Röntgen-Institut der Universität, Frankfurt a. M., Germany.)

Percutaneous introduction of two 20 mc seeds of Au^{198} into the sella results in necrosis of from $\frac{1}{4}$ to $\frac{1}{3}$ of the hypophyseal tissue. In 40 patients with progressive metastases this procedure has been done without mortality. Patients with painful vertebral metastases became free of pain almost immediately. In addition, regression of cerebral edema has been striking in several instances. This procedure has been used chiefly in metastasizing carcinoma of the breast, less often in patients with metastasizing prostatic or bronchial carcinomas, cerebral tumors and other malignancies. In an occasional patient whose response to the original implantation was only slight, 4 and even 6 such seeds have been implanted at a subsequent procedure.

Postoperative irradiation of cerebral tumors, particularly glioblastomata, was carried out by implanting approximately a dozen 10 mc Au^{198} seeds with the help of an image amplifier via surgical defects left in the skull at operation. Similar implantation was repeated once or twice subsequently. So few patients have been treated this way that no conclusions about effectiveness are possible.—*Henry G. Moehring, M.D.*

MEAD, K. W., and ROBERTSON, D. F. Radiation therapy in certain eye conditions. *Proc. Coll. Radiologists, Australasia*, Dec., 1957, *1*, 83–87. (From: Queensland Radium Institute, Brisbane, Australia.)

The authors present a summary of ten years' experience in treating limbal epithelioma, recurrent pterygium, vascularizing lesions of the cornea, Mooren's ulceration, and vernal conjunctivitis. Based on depth dose tables and clinical observation of radiation cataracts, the authors justify their preference for strontium 90 sources.

An unusual feature is their use of a tubular shield which serves as a lid retractor and guide into which the round strontium 90 plate is placed over the lesion. It also prevents any lateral flux of beta particles. Because the cornea and sclera are relatively radioresistant, the authors prefer single dose treatments.

Figures for cure rates are not presented except in the case of epitheliomata where the cure rate is practically 100 per cent. Sequelae, other than cataracts, the incidence of which was virtually abolished since the use of strontium 90, are not mentioned.—*P. J. Cavanaugh, M.D.*

HORST, WOLFGANG, HEYMANN, HANS-JOACHIM, and TEPE, HANS-JOACHIM. Über eine elektronische Methode zur Verbesserung des Kontrastes bei der Szintigraphie von Schilddrüse, Leber usw. (An electronic method for improving contrast in scintigrams of the thyroid gland, liver, etc.) *Strahlentherapie*, June, 1958, *106*, 191–210. (From: Universitäts-Strahleninstitut, Universitätskrankenhaus, Hamburg-Eppendorf, Germany.)

The authors give a general description of a scintigraphic system which permits suppression of a

variable intensity of impulses. Numerous illustrations demonstrate the improved contrast of "hot" and "cold" spots against the scintigrams of the thyroid gland or liver at large, when background (or even more) impulses are suppressed.—*Henry G. Moehring, M.D.*

MISCELLANEOUS

Johns, H. E. The roentgen and the rad and their use in radiology. *J. Canad. A. Radiologists*, June, 1958, *9*, 36–39. (From: Division of Physics, Ontario Cancer Institute, University of Toronto, Toronto, Ontario.)

In an attempt to establish a practical universal unit of radiation dosimetry, the International Commission on Radiological Units recommended in Copenhagen, in 1953, the acceptance of a unit of absorbed dose, the "rad."

Confusion in the use of the roentgen has arisen from the dual interpretation of its definition, *i.e.*, "the quantity of X or gamma radiation such that the associated corpuscular emission per 0.001293 grams of air, produces, in air, ions carrying 1 e.s.u. of quantity of electricity of either sign."

One interpretation is that the roentgen was defined as the unit which characterizes the output of a roentgen ray machine or characterizes the radiation coming from a radioactive source. Another is that the roentgen can be used as a unit of energy absorbed. One roentgen given to one gram of air corresponds to an energy absorption of 87.7 ergs (a new figure based on W = 34 e.v./ion pair). This conversion factor is constant for all energies of the radiation. One roentgen given to one gram of water corresponds to an energy absorption of about 97.7 ergs, but this conversion factor varies as the energy of the radiation is changed. The conversion factor to obtain absorption in a biologic material, such as bone or fat, varies over rather wide limits as the energy is changed.

To clarify these two concepts, the Commission has recommended that the "roentgen" be a unit of exposure dose characterizing what comes from the machine and measured by its ability to ionize air, and that the "rad" be a unit of absorbed dose equal to 100 ergs/gm. characterizing the radiation absorbed in the biologic material of interest and imparting energy to matter by ionizing particles per unit mass.

The author points out that the "absorbed dose" has great practical advantage and accuracy over the "exposure dose" when one is determining the exact amount of ionization that has taken place in the build up region between the skin surface and point of maximum in the subcutaneous tissues, bone and fat. For energies greater than 3 mev. calculation of absorbed dose from a beta emitting radioactive material, in terms of the concentrations in mc/gm. is also easy. The number of disintegrations per second multiplied by the mean energy of the disintegration gives the energy absorbed in ergs/gm. This divided by 100 expresses the dose in rads.

The conversion factors from roentgens to rads vary with the tube potential, filter, half-value layer and radiation spectrum. For water and muscle, the conversion factors do not vary much from the average value of about 0.96. For bone the factor varies widely and based on the half-value layer, in the range from 0.5 mm. Cu to 4.0 mm. Cu, shows a variation from 2.05 to 1.10, respectively.

For detailed study of this highly significant and practical advance in radiation dosimetry, the reader is referred to the original article and to the Report of the International Commission on Radiological Units and Measurements (ICRU), 1956, Handbook 62, National Bureau of Standards, Washington, D. C.—*Donald Monson, M.D.*

Bertram, Claus, and Höhne, Günter. Über die Mutationsauslösung mit schnellen Elektronen. (The production of mutations with fast electrons.) *Strahlentherapie*, June, 1958, *106*, 269–272. (From: Universitäts-Frauenklinik, Hamburg-Eppendorf, Germany.)

The rate of production of sex-linked, recessive, lethal mutations in Drosophila was determined by the Muller-5′(Basc-) method after administration of 4,000 and 2,000 r of conventional roentgen rays (200 kv., 20 ma.) and of 4,000 and 2,000 rep of an electron beam (15.5 mev.) from the betatron.

No statistically significant difference in the rate of production of the mutations was demonstrated between these 2 types of ionizing radiation; *i.e.*, the biologic effect of conventional roentgen rays and of fast electrons was equal when measured by this method.—*Henry G. Moehring, M.D.*

Norwood, W. Daggett. Common sense approach to the problem of genetic hazard due to diagnostic radiology; report based in part on study of exposures in a small American industrial city. *J.A.M.A.*, Aug. 16, 1958, *167*, 1928–1935. (Address: 1936 Harris Ave., Richland, Wash.)

This article is based in part on a study of exposures in a small industrial city, Richland, Washington, the resident community of the Hanford Atomic Products Operation. Discussions and publicity concerning the amount and effect of radiation due to fall-out from testing atomic weapons have made the American public more aware of the hazards of radiation. Considering the relative genetic hazards to whole populations from man-made radiation, it is stated that by far the largest contribution comes from diagnostic radiology. At the same time, it should be noted that the judicious use of diagnostic radiology is one of medicine's most important tools.

Realization that radiation increases the mutation

rate dates back 30 years to Muller's experiments with fruit flies. Concern has been heightened by recent findings that exposure of mice to a given quantity of radiation increases the mutation rate by about 15 times as much as does an equal exposure of Drosophila, which had formerly served as the sole basis for inferring human risks. It should be remembered that there are many factors other than radiation which cause genetic changes in laboratory animals, and presumably in man, such as temperature, oxygen tension, and various chemicals. Based on data from fruit flies and the fact that wearing of clothes increases male gonad temperature by 3°C, Ehrenberg and co-workers feel that wearing clothes may cause almost half of the present load of spontaneous mutations. They recommend the wearing of kilts.

It is noted that employee exposure due to diagnostic radiology is considerably increased by the practice of routinely taking roentgenograms of all male applicants for employment, particularly roentgenograms of backs, unless the gonads are protected by shielding. Chest roentgenograms add very little to gonad exposure, and even this could be eliminated by a simple curtain type of shielding. They do add to local regional exposure, however. In a phantom study, using 14×17 inch film, the lung dose was 10 mr per film, while it was 400 mr when the photofluoroscopic technique and a 4×5 inch film were used. For this reason, 14×17 inch films with standard technique are used for annual chest roentgenographic examinations on employees at the Hanford Operation who have potential exposure at work.

This discussion attempts to present a common sense approach in limiting exposure to the gonads without sacrificing the tremendous value of diagnostic roentgenologic examinations. Following the recommendations in Handbook 60 on x-ray protection, prepared by the NCRP (National Committee on Radiation Protection), will aid greatly in reducing exposure to patients, technicians, and physicians. The most important steps are accurate limiting (coning) and filtering of the primary roentgen ray beam; use of the most sensitive combination of film, screens, developing chemicals, and temperature; use of the highest voltage that will permit a satisfactory film contrast; and reduction to a minimum of the number of films and screening time of each examination. Electroluminescence, a new kind of light useful for image intensification, may reduce radiation exposure in fluoroscopy by a factor of 30, when equipment becomes available. Gonads should be protected, when possible, by appropriate screening devices. Special care should be taken during examinations of any anatomic portion of infants or small children to avoid, if at all possible, catching the gonads in the primary beam. The patient is so small that the gonads are closer to every area that may be examined.

It is noted that Moeller and associates estimated, in 1953, that there were 125,000 roentgen ray machines in the United States. One-half of these belong to dentists and hospitals, the other half to doctors, osteopaths, chiropodists, and chiropractors. Better understanding is needed on the part of some members of this group in order that they may improve installations and techniques and enhance their judgment in ordering roentgenographic examinations, which are in the best interest of the patient, after carefully weighing all factors.

Other items of interest in this article include a discussion of quantitative estimates of genetic damage, discussions of aging due to radiation and new permissible limits for population exposures, a detailed study of all diagnostic procedures performed in Richland, Washington, for a four year period, and results of phantom studies to determine depth doses for roentgenographic procedures.—*D. S. Kellogg, M.D.*